VOLUME 34 SEPTEMBER 1956 NUMBER 9

Canadian Journal of Chemistry

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OTTAWA CANADA

CANADIAN JOURNAL OF CHEMISTRY

(Formerly Section B, Canadian Journal of Research)

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Canadian Journal of Chemistry

Issued by THE NATIONAL RESEARCH COUNCIL OF CANADA

VOLUME 34 SEPTEMBER 1956 NUMBER 9

THE CONDENSATION OF FURAN AND SYLVAN WITH SOME CARBONYL COMPOUNDS[1]

BY W. H. BROWN[2] AND H. SAWATZKY[3]

ABSTRACT

Furan and sylvan condense with aldehydes, chlorinated aldehydes and ketones, and keto acids, in the presence of hydrochloric acid. In most cases, the corresponding difurylalkane or difuryl-substituted acid is formed. In special cases the reaction stops at the furylcarbinol stage.

Difurylalkanes have been accessible, in the past, only through a variety of indirect approaches. Thus, for example, difurylmethane (V) has been prepared by Reichstein, Grussner, and Zschokke (7) by the reduction of difuryl ketone. Gilman and Wright (5) synthesized the same substance by the interaction of 2-chloromercurifuran and furfuryl chloride. Dinelli and Marini (3) treated ethyl furoate with trioxane in the presence of sulphuric acid. By subsequent saponification, hydrolysis, and decarboxylation they obtained difurylmethane. This compound has also been isolated as a product during the acid-catalyzed resinification of furfuryl alcohol (4, p. 222).

Recently, Ackman, Brown, and Wright (1) have reported the formation of 2,2-difurylpropane by the condensation of furan with acetone in the presence of hydrochloric acid. Other methyl ketones gave analogous products.

In the present investigation, it has been found that furan also condenses with aldehydes, chlorinated aldehydes and ketones, and keto acids. The condensation products are difurylalkanes in the case of aldehydes and ketones. With keto acids, the corresponding difuryl-substituted acids result. Chlorinated aldehydes and ketones, when condensed with furan, yield chlorinated difurylalkanes in some cases, while in others, unstable products, thought to be chlorinated furylcarbinols, are formed. Willard and Hamilton (8) have already reported the condensation of furan (I) with chloral (VIII) to form 1-furyl-2,2,2-trichloroethanol (IX).

The investigation also includes the reaction of sylvan (2-methylfuran) (II) with the carbonyl compounds previously cited. Analogous products are obtained.

[1]*Manuscript received in original form December 30, 1955, and, as revised, May 25, 1956. Contribution from the Department of Chemistry, Ontario Agricultural College, Guelph, Ontario.*

[2]*Associate Professor of Chemistry, Ontario Agricultural College, Guelph, Ontario.*
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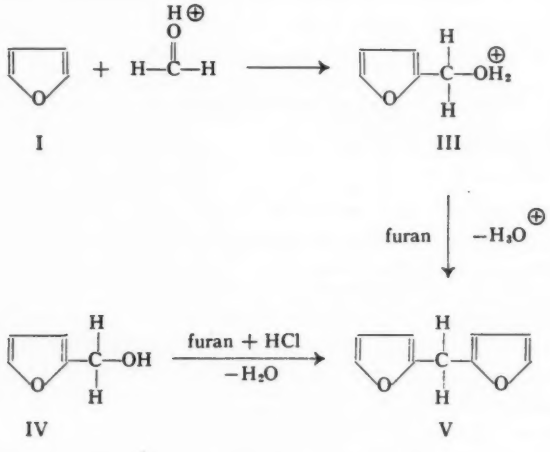
Tables I, II, and III show the specific carbonyl compounds concerned and data on the products formed.

When furan (I) is treated with aqueous formaldehyde solution in the presence of hydrochloric acid, difurylmethane (V) is formed in low (1.7%) yield. The identity of the product was established by mercuration according to the method of Gilman and Wright (5). A mixture melting point of this mercurial with the mercurial of difurylmethane, the latter prepared by the procedure of Dinelli and Marini (3), showed no depression.

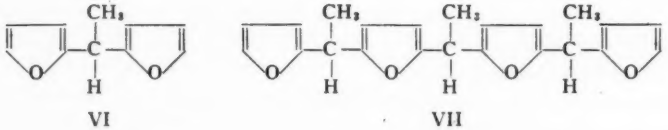
The proposed mechanism for the reaction is as follows:



I III IV V

It seems likely that protonated furfuryl alcohol (III) is an intermediate in the reaction, since furfuryl alcohol (IV), when treated with furan in the presence of hydrochloric acid, forms difurylmethane (V) in increased (15%) yield. No apparent reaction occurs between furfuryl alcohol and furan in the absence of acid. Other acidic compounds might also serve as catalysts (8).

In the reaction of acetaldehyde with furan, two products, 1,1-difurylethane (VI) and 1,1-*bis*[5-(methylfurfuryl)-furyl]ethane (VII), can be isolated.



VI VII

Here, again, the protonated furylcarbinol appears to be the intermediate, since 1,1-difurylethane (VI) is formed when methyl-furylcarbinol is treated with furan in the presence of hydrochloric acid.

Inspection of Table I shows that the yields of 1,1-disubstituted alkanes are

TABLE I

CONDENSATION PRODUCTS OF ALDEHYDES WITH FURAN AND SYLVAN

Reactants	Yield, %	B.p., °C./mm.	$n_D^{t°}$	$d_4^{20°}$	Molecular formula	Analysis	
						Calc.	Found
Furan and:							
Formaldehyde	1.7	79–81/12	1.4991/16	1.098	$C_9H_8O_2$		
Acetaldehyde	58	86–87/15	1.4993/20	1.073	$C_{10}H_{10}O_2$	C, 74.1; H, 6.21	C, 74.0; H, 6.05
	9.7	136–137/4	1.5218/20	1.105	$C_{18}H_{20}O_4$	C, 75.4; H, 6.33	C, 75.3; H, 6.44
Propionaldehyde	24	88–93/15	1.4930/20	1.047	$C_{11}H_{12}O_2$	C, 75.0; H, 6.87	C, 75.2; H, 7.33
Butyraldehyde	38	108/14	1.4890/20	1.015	$C_{12}H_{14}O_2$	C, 75.8; H, 7.42	C, 76.1; H, 7.58
Benzaldehyde	No reaction						
Furfural	No reaction						
Glyoxal	No reaction						
Sylvan and:							
Formaldehyde	34	114/15	1.5017/20	1.042	$C_{11}H_{12}O_2$	C, 75.0; H, 6.87	C, 75.6; H, 6.88
Acetaldehyde	61	113/12	1.4993/20	1.027	$C_{12}H_{14}O_2$	C, 75.7; H, 7.42	C, 75.8; H, 7.42
Propionaldehyde	63	118/14	1.4949/20	1.008	$C_{13}H_{16}O_2$	C, 76.4; H, 7.96	C, 76.8; H, 7.87
Butyraldehyde	73	132/15	1.4935/20	0.989	$C_{14}H_{18}O_2$	C, 77.0; H, 8.32	C, 77.0; H, 8.11

higher from sylvan than from furan. This points up the activating influence at the 2-position of an electron-donating group located on the 5-position of the furan nucleus (4, p. 27).

In Table II it may be seen that the presence of halogen in the carbonyl compound reduces the yield of the halogenated difurylalkane. The presence of

TABLE II

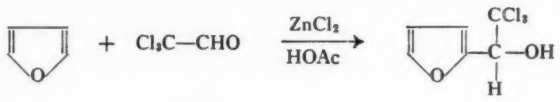
CONDENSATION PRODUCTS OF CHLORINATED ALDEHYDES AND KETONES WITH FURAN AND SYLVAN

Reactants	Yield, %	B.p., °C./mm.	$n_D^{20°}$	$d_4^{20°}$	Molecular formula	Analysis	
						Calc.	Found
Furan and:							
Chloroacetaldehyde		Decomposes			$C_8H_7O_2Cl$	Cl, 24.2	Cl, 22.3
Monochloroacetone	19	127–131/15	1.5208	1.170	$C_{11}H_{11}O_2Cl$	Cl, 16.9	Cl, 16.6
1,3-Dichloroacetone		Decomposes					
Sylvan and:							
Chloroacetaldehyde	11	142–144/14	1.5176	1.143	$C_{12}H_{13}O_2Cl$	Cl, 15.8	Cl, 15.7
Dichloroacetaldehyde		Decomposes					
Monochloroacetone	23	138–142/14	1.5160	1.115	$C_{13}H_{15}O_2Cl$	Cl, 14.9	Cl, 14.9
1,3-Dichloroacetone	5.2	175–179/14	1.5308	1.159	$C_{13}H_{14}O_2Cl$	Cl, 26.0	Cl, 26.0

an electron-donating group, such as methyl, either on the furan ring or in the carbonyl compound partially offsets the deactivating effect of chlorine in the carbonyl compound.

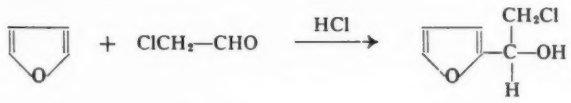
As shown by Willard and Hamilton (8), when furan (I) reacts with chloral (VIII) in the presence of zinc chloride and glacial acetic acid, the product is 1-furyl-2,2,2-trichloroethanol (IX) in fair yield. The inductive effect of the halogens decreases the basicity of the oxygen and to some extent increases the C—O bond strength by forcing participation of the unshared

electrons of oxygen in this bonding. Hence the OH becomes less likely to be protonated and thus less labile than in the unsubstituted cases.



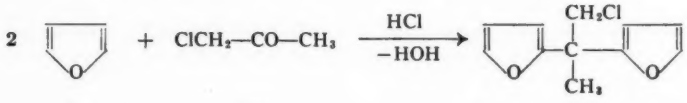
I VIII IX

In the case of some of the halogenated carbonyl compounds, the reaction with furan appears to have stopped at the carbinol stage. Thus, for example, furan (I) reacts with chloroacetaldehyde (X) to yield 1-furyl-2-chloroethanol (XI).



I X XI

However, when furan (I) and monochloroacetone (XII) are treated with hydrochloric acid the product of the reaction is 1-chloro-2,2-difuryl-propane (XIII). Here the methyl group is able to overcome the inhibiting action of the chlorine atom.



I XII XIII

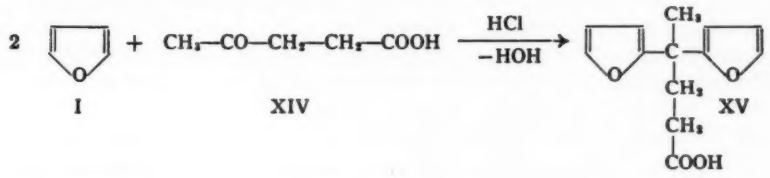
In the reaction of furan and sylvan with keto acids (Table III), some of the products are those which one would expect on the basis of normal reaction.

TABLE III

CONDENSATION PRODUCTS OF KETO ACIDS AND ESTERS WITH FURAN AND SYLVAN

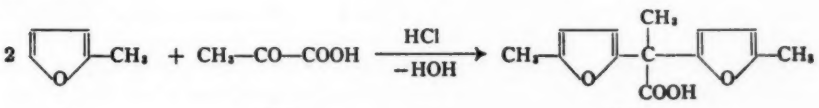
Reactants	M.p., ° C.	B.p., ° C./mm.	Yield, %	Molecular formula	Analysis	
					Calc.	Found
Furan and:						
Levulinic acid	68.5–69.5	180–220/17	29	$C_{13}H_{14}O_4$	N.E., 234	N.E., 232
Pyruvic acid	Gave only resins					
Ethyl acetoacetate		140–170/17	11 wt. %			
Sylvan and:						
Levulinic acid	84–85	207–230/16	33	$C_{13}H_{18}O_4$	C, 68.7; H, 6.91 N.E., 262	C, 69.1; H, 6.76 N.E., 261
Pyruvic acid	110.5–111.5		68	$C_{13}H_{14}O_4$	C, 66.6; H, 6.02 N.E., 234	C, 66.8; H, 6.11 N.E., 231
Acetoacetic acid		135–210/3	36 wt. %			
Ethyl acetoacetate		170–220/16	43 wt. %			

Thus, for example, furan (I) reacts with levulinic acid (XIV) to form γ-*bis*(furyl)-valeric acid (XV).



I XIV XV

While sylvan (II) reacts normally with pyruvic acid (XVI) to form α-*bis*(sylvyl)-propionic acid (XVII), furan reacts violently to yield a resinous product.



II XVI XVII

Both furan and sylvan react vigorously with ethyl acetoacetate in the presence of hydrochloric acid. The product in each case is an oil which does not lend itself readily to purification. These oils have not been investigated further.

Ackman, Brown, and Wright (1) prepared substituted tetroxaquaterenes by condensing difurylalkanes with the parent methyl ketones. In view of this, difurylmethane would be expected to condense with formaldehyde to form the unsubstituted tetroxaquaterene. Attempts to produce such a compound failed.

When 1,1-difurylethane (VI) and 1,1-*bis*[5-(methylfurfuryl)-furyl]ethane (VII) were treated with acetaldehyde in the presence of hydrochloric acid, resinous products were formed. No tetroxaquaterene formation occurred.

EXPERIMENTAL

All melting points have been corrected against reliable standards. Molecular weights were determined by Rast method. For the sake of brevity, only a few of the preparations are reported in operational detail. It may be assumed that the products listed in Tables I, II, and III may be obtained by following the procedure outlined for preparing a homologue.

Difurylmethane (*V*)

(*a*) *From Furan and Formaldehyde*

Into a 2-liter three-necked round-bottom flask fitted with a stirrer were introduced 50 ml. of 20% hydrochloric acid and 190 ml. (2.5 moles) of 36% aqueous formaldehyde solution. While cooling externally with tap water (14° C.), 170 gm. (2.5 moles) of furan was added dropwise over a period of 30 min. After five hours the reaction mixture was neutralized with solid sodium carbonate and then steam distilled. The distillate was extracted with ether, and the ether solution washed with 28% aqueous ammonia solution to remove

formaldehyde and then with water to remove ammonia. The ether solution, after being dried over anhydrous magnesium sulphate, was evaporated. The residual oil was distilled under diminished pressure giving 3.10 gm. (1.7%) of a colorless oil, b.p. 79–81° C. (13 mm. Hg); $\eta_D^{16°}$ 1.4991; $d_{4°}^{20°}$ 1.098. Physical constants reported for difurylmethane (4, p. 78) are: b.p. 78° (12 mm. Hg); $\eta_D^{20°}$ 1.5049; $d_{4°}^{20°}$ 1.102.

(*b*) *From Furan and Furfuryl Alcohol*

In a 125 ml. Grignard-type flask, fitted with a stirrer, were placed 17 gm. (0.25 mole) of furan, 24.5 gm. (0.25 mole) of furfuryl alcohol, and 5 ml. of 37% hydrochloric acid. The mixture was cooled to 13° C. and stirred vigorously for four hours at this temperature. When the reaction mixture was worked up according to the procedure outlined in (*a*), 5.65 gm. (15%) of a colorless oil was obtained. This oil had identical physical constants with the oil described in (*a*).

Both oils were shown to be identical by mixture melting point of their mercurials, m.p. 149.5°, prepared by the method of Gilman and Wright (5). A mixture melting point of these mercurials with the mercurial of difurylmethane, m.p. 149.5°, the latter prepared by the procedure of Dinelli and Marini (3), showed no depression.

1,1-Difurylethane (*VI*)

(*a*) *From Furan and Methyl-furylcarbinol*

To 0.2 mole of methyl-furylcarbinol Grignard complex, prepared *in situ* by the method of Peters and Fischer (6), was added 17 gm. (0.25 mole) of furan. The ice-cold mixture was stirred while 100 ml. of water was added, and the resulting mixture treated with 37% hydrochloric acid until 5 ml. were in excess. After it had been stirred for two and one-half hours the reaction mixture was neutralized with solid sodium carbonate and steam distilled. The oil obtained by this procedure distilled at 84–87° C. (15 mm. Hg), and weighed 7.3 gm. (22%); $\eta_D^{20°}$ 1.5003; $d_{4°}^{20°}$ 1.072.

(*b*) *From Furan and Acetaldehyde*

In a 250 ml. Grignard-type flask, fitted with a stirrer, were placed 20 ml. of 37% hydrochloric acid, 20 ml. of water, and 136 gm. (2.0 mole) of furan. After the flask had been cooled externally with tap water at 15° C., 44 gm. (1.0 mole) of acetaldehyde was added dropwise over a period of 100 min. Stirring at 15° C. was continued for 17 hr. At the end of this time, 200 ml. of water was added to the mixture which was then made alkaline by the addition of saturated sodium bicarbonate solution. After it was extracted with 200 ml. of ether, the ether solution was separated, washed with 100 ml. of water, and dried over anhydrous sodium sulphate. After the ether was flashed off, the residual brown oil was fractionated in a column as described by Bower and Cooke (2). The first fraction was a colorless oil weighing 94.5 gm. (58%) and boiling at 86–87° C. (15 mm. Hg); $\eta_D^{20°}$ 1.4993; $d_{4°}^{20°}$ 1.073. Anal. Calc. for $C_{10}H_{10}O_2$ (162.18): C, 74.1; H, 6.21. Found: C, 74.0; H, 6.05.

It is important that the order of addition of reagents to the flask be as indicated. If the acetaldehyde is mixed with the acid, and furan added subsequently, paraldehyde is the chief product.

1,1-bis[5-(Methylfurfuryl)-furyl]ethane (VII)

A second fraction from the preceding distillation, a pale yellow oil, boiled at 136–137° C. (3–4 mm. Hg). It weighed 11.3 gm. (9.7%); $n_D^{20°}$ 1.5218; $d_{4°}^{20°}$ 1.105. Anal. Calc. for $C_{22}H_{22}O_4$: C, 75.4; H, 6.33; mol. wt., 350. Found: C, 75.3; H, 6.44; mol. wt., 330.

1-Chloro-2,2-difurylpropane (*XIII*)

In a 250 ml. Grignard-type flask, fitted with a stirrer, were placed 34 gm. (0.5 mole) of furan, 23 gm. (0.25 mole) of monochloroacetone, and 10 ml. of 20% hydrochloric acid. The mixture was stirred for 55 hr. at 20° C. A greenish viscous mass formed. After it was neutralized with solid sodium carbonate the mixture was steam-distilled. The colorless oil obtained in this manner distilled at 127–128° C. (15 mm. Hg). It weighed 10.0 gm. (19%) and had $n_D^{20°}$ 1.5208; $d_{4°}^{20°}$ 1.170. Anal. Calc. for $C_{11}H_{11}O_2Cl$ (210.60): Cl, 16.9. Found: Cl, 16.6.

α-bis(Sylvyl)-propionic acid (*XVII*)

In a 250 ml. Grignard-type flask, fitted with a stirrer, were placed 22 gm. (0.25 mole) of pyruvic acid, 41 gm. (0.50 mole) of sylvan, and 5 ml. of 37% hydrochloric acid. The mixture evolved heat and was cooled to 11° C. while stirring for two hours, at which time it was partially neutralized with sodium carbonate. A solid weighing 40 gm. (68%) formed.

The acid was difficult to purify, but repeated crystallization from acetone–hexane gave light brown cubes, m.p. 110.5–111.5° C. Anal. Calc. for $C_{13}H_{14}O_4$: C, 66.6; H, 6.02; N.E., 234. Found: C, 66.8; H, 6.11; N.E., 231.

ACKNOWLEDGMENTS

We wish to express our gratitude to Canadian Industries Limited for financial aid to one of us (H.S.).

We are indebted to the du Pont Company of Canada for generous supplies of furan and to Mr. G. Bedrosian for technical assistance.

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THE OXIDATION OF HYDRAZOBENZENE BY AMMONIUM PERSULPHATE IN ACETONITRILE–WATER SOLUTION[1]

By B. J. P. Whalley, H. G. V. Evans, and C. A. Winkler

ABSTRACT

In a given experiment, second order kinetics were displayed during the greater part of the reaction over a considerable range of initial concentrations of reactants. In general, the second order behavior was maintained to greater extent of reaction when hydrazobenzene was in excess. The calculated second order rate constant, k, decreased with increase in initial hydrazobenzene concentration and increased with increase in initial concentration of ammonium persulphate. For different equimolar concentrations of reactants, k was virtually independent of initial concentrations. The value of k was proportional to the square root of the ratio of the initial concentrations of persulphate and hydrazobenzene. The activation energy of the over-all reaction was 16 kcal. per mole. A free radical mechanism appears to account reasonably well for the major experimental observations.

INTRODUCTION

The oxidation of mercaptans by potassium persulphate in glacial acetic acid – water solution has been discussed in a previous paper from this laboratory (3). In respect of persulphate disappearance, the reaction was found to change from first to second order as the mercaptan concentration was reduced to a sufficiently low value. The calculated first order constant decreased with increase of persulphate concentration, but was independent of the chain length of the aliphatic mercaptan used. A secondary salt effect was observed; sulphate ions and sulphuric acid increased the rate, while potassium ions retarded it. An activation energy of 26,000 cal. per mole was found for the reaction. The experimental data were explained by a mechanism involving the attack on mercaptan by sulphate ion radicals formed by thermal decomposition of persulphate ions. Although Levitt (6) has recently suggested that the data could be more satisfactorily interpreted if sulphur tetroxide rather than the sulphate ion radical were considered the reactive entity, Eager and McCallum (2) have shown by radioactive evidence that such a mechanism is untenable.

Bartlett and Nozacki (1) have found that the addition of methanol to a buffered aqueous solution of persulphate largely increased the rate of persulphate decomposition. The rate was found to be three-halves order in persulphate and half order in methanol. The results appear to be satisfactorily explained by a free radical mechanism, in which the initial formation of sulphate ion radicals resulted from the direct reaction of persulphate with methanol rather than unimolecular decomposition of persulphate. Bartlett's mechanism has been challenged by Kolthoff *et al.* (5) since the addition of allyl acetate virtually eliminates the rapid disappearance of persulphate in the presence of methanol.

[1]*Manuscript received April 23, 1956.*
Contribution from the Physical Chemistry Laboratory, McGill University, Montreal, Quebec, with financial assistance from the National Research Council.

The present study was made with a view to obtaining further information about the oxidation of organic molecules by persulphate in homogeneous systems, particularly when the organic reactant is one that might be considered exceedingly susceptible of oxidation. To this end hydrazobenzene was chosen as the substrate.

EXPERIMENTAL AND RESULTS

The glacial acetic acid – water solvent used in the previous study with mercaptans was unsatisfactory for present purposes, owing to the formation of a blue-black coloration, followed by a dark precipitate, when hydrazobenzene was added to the solution of persulphate. A mixed solvent consisting of 100 ml. acetonitrile and 12.5 ml. water was found to be satisfactorily stable under the experimental conditions it was desired to use; at 25° C., the rate of disappearance of ammonium persulphate (0.0015 *M*) in the solvent was negligible, while at 45° C., a rate of only 0.3% per hour was measured when the initial concentration was 0.006 *M*.

Technical grade acetonitrile (Brickman and Co., Montreal) was dried over sodium sulphate and distilled through a Widmer column. The fraction boiling between 82.0° and 82.5° C. was collected. It was found that acetonitrile once distilled in this way gave rate data that were within 5% of values obtained when doubly distilled solvent was used; hence for practically all the experiments the acetonitrile was distilled only once.

Distilled water that had been redistilled through a quartz condenser was used for most of the work, although regular laboratory distilled water from a Barnstead still was found to give equally good results.

Ammonium persulphate, reagent grade, from Brickman and Co., Montreal, was used as received. It was stored in brown bottles in a vacuum desiccator over sulphuric acid.

Hydrazobenzene was obtained from the same company and stored under vacuum. Before use, it was recrystallized from ethanol and washed with ice-cold 50% ethanol–water until the filtrate showed no yellow color. The pure white crystals were immediately transferred to a vacuum desiccator and pumped dry with a high vacuum pump. The melting point of the purified material was invariably sharp at 126.5° C. (uncorr.).

The rate of reaction between hydrazobenzene and persulphate was measured by determining the rate of formation of azobenzene with a Fisher Electrophotometer. Formation and intensification of a yellow color in the solution was shown to be due to azobenzene by comparing the absorption spectrum of a reaction mixture after about 10% reaction with that for azobenzene in acetone, using a Beckman spectrophotometer, model DU. For analytical purposes, the electrophotometer was calibrated against solutions of azobenzene of known concentrations in the acetonitrile–water solvent.

Some experiments were made in which the sulphuric acid formed during reaction was titrated with standard base. This method of following the reaction was only approximate, owing to a difficult end point in the yellow reaction mixture. Phenol red was the only indicator found to be at all satisfactory.

Attempts to follow the disappearance of persulphate by the volumetric method of Kolthoff *et al.* (4) were unsuccessful, owing to some undetermined effect of hydrazobenzene; differential potentiometric titrations (7) also were unsuccessful.

Preliminary experiments indicated that hydrazobenzene was rapidly oxidized when a solution of it in acetonitrile–water was exposed to air. Hence, experimental conditions were arranged to minimize the amount of oxygen in the solvent and entrained in the solid reactants. Acetonitrile was deoxygenated by refluxing it for half an hour, after which it was cooled and stored under a positive pressure of oxygen-free nitrogen. Distilled water was deoxygenated with a stream of oxygen-free nitrogen and stored under a positive pressure of the gas. By suitable techniques for sweeping with oxygen-free nitrogen it was possible to prevent contamination of the reaction mixture with oxygen while it was being made and while samples were being taken for analysis. Checks were made for oxygen contamination with blank experiments (no persulphate present) under the same conditions and at the same time that each series of experiments with persulphate was in progress. At no time was any correction necessary for oxidation due to oxygen.

In a preliminary experiment with hydrazobenzene in excess over persulphate (0.024 *M* and 0.0060 *M* respectively) it was found that when reaction was complete the yield of azobenzene was within 2.5% of the amount that should be formed if one mole of persulphate oxidized one mole of hydrazobenzene. The stoichiometry of the reaction may therefore be represented

$$S_2O_8^{=} + (C_6H_5NH)_2 \rightarrow 2HSO_4^{-} + (C_6H_5N)_2.$$

Experiments were made to determine the order of the reaction and the effect on specific rate of varying the initial reactant concentrations. The data were found to conform best to a second order rate equation, and are presented accordingly.

In Fig. 1 are shown some typical second order plots for different initial concentrations of hydrazobenzene at given (0.0060 *M*) initial persulphate concentration. The increase in calculated second order rate constant towards the end of reaction was observed in most of the experiments. In general, it appeared that, when either hydrazobenzene or ammonium persulphate concentration was held constant at 0.006 *M*, and the concentration of the other increased, second order linearity tended to be preserved to larger extents of reaction. This seemed to be particularly true when hydrazobenzene was the reactant in excess. At persulphate concentrations below 0.006 *M*, second order linearity appeared to exist to larger extents of reaction when hydrazobenzene concentrations were correspondingly low. The dependence of extent of linearity on which of the reactants was in excess was more pronounced at higher than at lower temperatures.

The calculated second order rate constant was dependent upon initial concentration of the reactants in the manner shown in Table I and Fig. 2. Although the results were generally reproducible within about 5% at the higher concentrations, they tended to be more variable as the concentrations

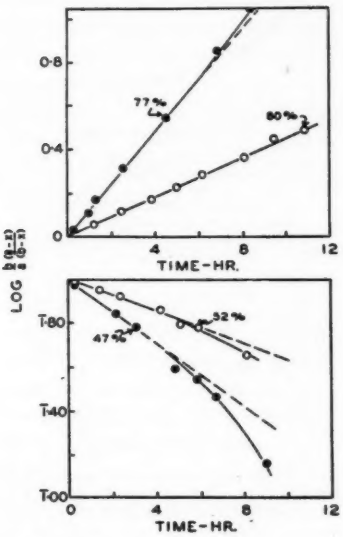

FIG. 1. Typical second order plots.
Temp. 25.02±0.02°C.
Initial concentration ammonium persulphate, 0.00600 mole/liter.
Initial concentration hydrazobenzene:
Upper frame: ●—0.0120 mole/liter.
○—0.0240 mole/liter.
Lower frame: ●—0.00300 mole/liter.
○—0.00150 mole /liter.

TABLE I

EFFECT OF DIFFERENT INITIAL CONCENTRATIONS OF HYDRAZOBENZENE AND AMMONIUM PERSULPHATE ON THE CALCULATED SECOND ORDER RATE CONSTANT

Hydrazobenzene, M./l.	Ammonium persulphate = 0.006 M./l. k (l. m.$^{-1}$ hr.$^{-1}$)			Ammonium persulphate, M./l.	Hydrazobenzene = 0.006 M./l. k (l. m.$^{-1}$ hr.$^{-1}$)		
	25.02± 0.01°C.	35.28± 0.01°C.	45.75± 0.02°C.		25.02± 0.01°C.	35.28± 0.01°C.	45.75± 0.02°C.
0.00150	40	118		0.00063			59
0.00155	37			0.0015	14	36	
0.0030	24	66	143	0.0030	18	45	101
0.0030	35			0.0060	20	43	115
0.0030	28			0.0060	20	45	118
0.0060	20	43	115	0.012		47	135
0.0060	20	45	118	0.015	22		143
0.012	17	42	91	0.015	21		
0.012	17			0.024		62	
0.018	18			0.030	24		
0.018	16			0.031	25		
0.020	—	39					
0.024	15						
0.030	—	32	79				
0.0395	9						

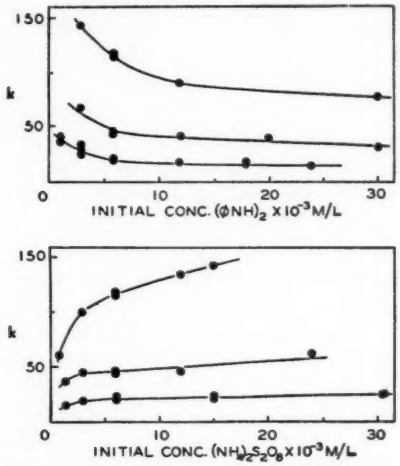

FIG. 2. Dependence of second order rate constant on initial concentration of the reactants.
Upper frame: Initial concentration of ammonium persulphate, 0.00600 mole/liter.
Lower frame: Initial concentration of hydrazobenzene 0.00600 mole/liter.
Temperatures: top curves, 25.02°C.
middle curves, 35.28°C.
bottom curves, 45.75°C.

were reduced. However, there appears to be no doubt that the changes in k represented by Fig. 2 are real.

When experiments were made at 25° C. with equimolar concentrations lower than 0.006 M, the rates were relatively independent of concentration of the reactants, as indicated by the following data:

Initial concn. of hydrazobenzene and ammonium persulphate (M./l.)	k (l. m.$^{-1}$ hr.$^{-1}$)
0.0015	20
0.0030	22
0.0045	20
0.0060	20

Two experiments made at 0° C. with 0.0060 M persulphate gave the following results:

Initial concn. of hydrazobenzene (M./l.)	k (l. m.$^{-1}$ hr.$^{-1}$)
0.0060	1.7
0.036	1.4

These data, together with those of Table I, were used to calculate the activation energy for the reaction at different relative concentrations of the

two reactants. There appeared to be no significant change of activation energy with initial concentration of reactants, and a value of 16±0.5 kcal. per mole may be assigned to the over-all reaction.

An attempt to determine the effect of added sulphuric acid on the reaction rate was frustrated by the almost immediate formation of a white precipitate in the reaction mixture. A similar precipitate, determined in one experiment by filtration and weighing to amount to about 3% of the hydrazobenzene and 2% of the persulphate taken, was observed in most of the reaction mixtures as reaction approached completion. This precipitate was insoluble in acetonitrile and in water, and did not melt below 300° C. Its identity was not established, since it represented such a small proportion of the reactants consumed.

Three experiments were made in which the increase in titratable acid in the reaction mixture was followed simultaneously with photometric determinations of the azobenzene formed. The initial concentrations of hydrazobenzene and ammonium persulphate were 0.0060 *M* and 0.0060 *M*, 0.0090 *M*, and 0.012 *M* respectively. As indicated earlier, the acidity determinations were rather approximate but all three experiments showed that less titratable acid was formed than would be expected from the amount of hydrazobenzene consumed. The deficit amounted to 15–20%.

DISCUSSION

Although the stoichiometry and the reasonably good second order kinetic behavior of the reaction might be interpreted in terms of a single step oxidation, it seems more probable (8) that at least two single electron transfer steps are involved. In view of this, the following reaction sequence is suggested:

$$S_2O_8^{=} + C_6H_5NHNHC_6H_5 \xrightarrow{k_1} HSO_4^{-} + C_6H_5NH\dot{N}C_6H_5 + SO_4^{\cdot-}$$

$$SO_4^{\cdot-} + C_6H_5NHNHC_6H_5 \xrightarrow{k_2} HSO_4^{-} + C_6H_5NH\dot{N}C_6H_5$$

$$S_2O_8^{=} + C_6H_5NH\dot{N}C_6H_5 \xrightarrow{k_3} HSO_4^{-} + SO_4^{\cdot-} + C_6H_5NNC_6H_5$$

$$2C_6H_5NH\dot{N}C_6H_5 \xrightarrow{k_4} C_6H_5NHNHC_6H_5 + C_6H_5NNC_6H_5$$

The scheme neglects a possible reaction, viz.

$$SO_4^{\cdot-} + C_6H_5NH\dot{N}C_6H_5 \rightarrow HSO_4^{-} + C_6H_5NNC_6H_5,$$

inclusion of which makes mathematical treatment difficult.

If, for ease of representation, $P = S_2O_8^{=}$, $H = C_6H_5NHNHC_6H_5$, $A = C_6H_5NNC_6H_5$, the usual steady state assumptions give the rate of formation of azobenzene as

$$\frac{dA}{dt} = k_3[P]\sqrt{\frac{k_1}{k_4}[H][P]} + k_1[H][P] \qquad [1]$$

$$= k_1[H][P]\left(\frac{k_3}{\sqrt{k_1k_4}} \cdot \sqrt{\frac{[P]}{[H]}} + 1\right) \qquad [2]$$

However, because of the apparent second order kinetics of the greater part of most of the reactions, the usual second order rate equation was assumed to be applicable, that is:

$$[3] \qquad \frac{dA}{dt} = k\,[H][P],$$

where k is the calculated second order rate constant recorded in Table I and Fig. 2. Hence,

$$[4] \qquad k = k_1\left(\frac{k_3}{\sqrt{k_1 k_4}} \cdot \sqrt{\frac{[P]}{[H]}} + 1\right)$$

or

$$k \propto \sqrt{[P]/[H]}.$$

Equation [4] predicts, for a reaction scheme of the type postulated, that the calculated second order rate constant, k, should be large for relatively large concentrations of persulphate, small for relatively large concentrations of hydrazobenzene, and independent of concentration for equimolar concentrations of the two reactants. All of these conditions were realized experimentally.

In Fig. 3 are plotted the values of k against $\sqrt{[P]/[H]}$. Extrapolation of

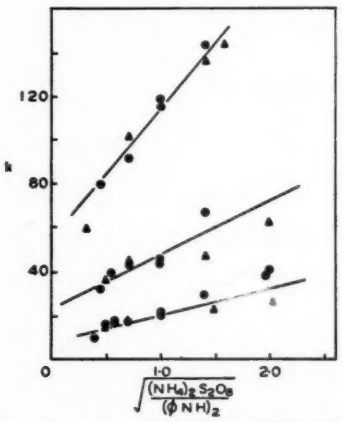

FIG. 3. Plots of second order rate constant against $\sqrt{[\text{Persulphate}]/[\text{Hydrazobenzene}]}$.
●—Initial concentration ammonium persulphate, 0.00600 mole/liter.
▲—Initial concentration hydrazobenzene, 0.00600 mole/liter.
Temperatures for lower, middle, and upper curves were 25.02°, 35.28°, and 45.75°C. respectively.

these lines to zero gave values of k_1, the second order rate constant for the attack of hydrazobenzene by persulphate ion, the chain initiation step, at the three temperatures. The values so obtained were:

T (°K.)	k_1 (l. m.$^{-1}$ hr.$^{-1}$)
298.0	7.5
308.3	23.0
318.8	54.0

These values give a very satisfactory Arrhenius line, corresponding to an activation energy of 17.5 kcal./mole.

It should be mentioned, perhaps, that conductance measurements indicated ammonium persulphate in the acetonitrile–water solvent used to be only weakly ionized. Hence, true persulphate ion concentrations in the reaction mixture would be less than values used in the calculations and plots. The discrepancy would be the less, the higher the temperature. Unfortunately, correction of the persulphate concentration was not possible since, as usual with weakly ionized solutes, curvature of the relation between equivalent conductance and square root of the concentration did not permit evaluation of the conductance at infinite dilution, hence the degree of dissociation.

To determine whether the rate constant k_1 evaluated from individual experiments would be independent of initial concentration of reactants (to replace the concentration dependent k), equation [2] was integrated to yield

$$[5] \qquad k_1 t \frac{([P]-[H])}{2} = \ln \frac{\sqrt{[H]/[P]}+k_5}{\sqrt{([H]-x)/([P]-x)}+k_5}$$

or

$$[6] \quad k_1 t = \left\{\frac{2}{[P]-[H]} \cdot \ln\left(\sqrt{\frac{[H]}{[P]}}+k_5\right)\right\} - \left\{\frac{2}{[P]-[H]} \cdot \ln\left(\sqrt{\frac{[H]-x}{[P]-x}}+k_5\right)\right\}$$

where $k_5 = k_3/\sqrt{k_1 k_4}$ and k_1 is the rate constant for the initiation step.

Expansion of equation [6] gives

$$[7] \quad k_1 = \left\{\frac{2}{([P]-[H])t} \cdot \ln \frac{(1-x/[P])}{(1-x/[H])}\right\} + \left\{\frac{2k_5}{([P]-[H])t}\left(\sqrt{\frac{[P]}{[H]}}-\sqrt{\frac{[P]-x}{[H]-x}}\right)\right\} + \ldots = 2k+2k_5A.$$

Values of k and A were calculated for different times in a given experiment at 25.02° C. for various initial concentrations of the reactants, and average values of the two quantities obtained.

From a plot of k against A, a value for k_5 at 25.02° C. of 0.6 was obtained. This value of k_5 was put into Equation [6] and the second term on the right-hand side of this equation was plotted against time for various concentrations of hydrazobenzene and persulphate. From the slopes of these plots, values of k_1 were obtained and these in turn were plotted against initial concentrations of hydrazobenzene and persulphate, with the results shown in Fig. 4. The superiority of k_1 over k in respect of dependence on initial concentration (cf. Figs. 2 and 4) is sufficient perhaps to indicate that the approach outlined is sound. A more satisfactory test would have been possible if sufficient data had been available at the higher temperatures, but unfortunately it was not possible to obtain a satisfactory evaluation of the necessary quantities with the data recorded for these temperatures.

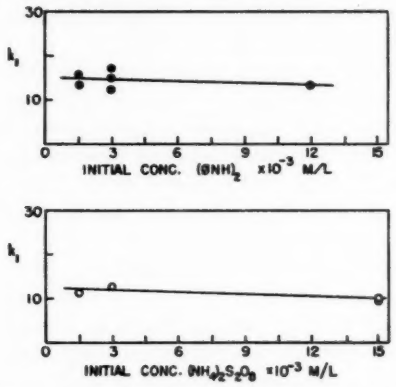

FIG. 4. Effect of different concentrations of hydrazobenzene on k_1, the corrected rate constant.
Temp. 25.02°C.
Upper frame: Initial concentration ammonium persulphate, 0.00600 mole/liter.
Lower frame: Initial concentration hydrazobenzene, 0.00600 mole/liter.

The second order kinetics displayed in individual experiments for considerable variation in initial concentrations of reactants would indicate that a compensation existed in the reaction to modify the behavior predicted by the relation $k \propto \sqrt{[P]/[H]}$. It is inherent in this relation that in a given experiment, unless the reactants are in equimolar concentrations, the calculated specific rate should decrease during the course of reaction when hydrazobenzene is in excess and increase when persulphate is in excess. Actually, the deviations from linearity were always in the direction of apparent increase in specific rate. Much of the compensation might have been due to an increased dissociation of persulphate as its consumption progressed, but it seems likely that some other factor or factors not yet identified also contributed to the observed behavior.

The interpretation of the experimental data suggests that the reaction is initiated by the formation of sulphate ion radicals resulting from direct attack by persulphate ions rather than by sulphate ion radicals from unimolecular decomposition of persulphate.

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PREPARATION AND PROPERTIES OF CRYSTALLINE CANDIDIN[1]

By L. C. Vining and W. A. Taber

ABSTRACT

Candidin, the antifungal antibiotic produced by *Streptomyces viridoflavus*, has been isolated in crystalline form. Analyses and equivalent weight values best fit a molecular formula $C_{46}H_{75}NO_{17}$. The substance is amphoteric and probably contains one carboxyl and one amino group. Infrared spectral evidence also indicates a polyhydroxylated structure, and the absorption in the visible region shows the presence of a conjugated heptaene chromophore. An additional conjugated diene elsewhere in the molecule is suggested by hydrogenation values and the absorption maximum at 228 mμ.

The isolation from *Streptomyces viridoflavus* of a new antibiotic active primarily against fungi was first reported in 1953 (5). The light absorption spectrum and chemical properties of this substance were very similar to candicidin (2), but it was shown to differ both in its behavior upon countercurrent distribution, and by the higher activity exhibited against filamentous fungi.

Subsequently both candidin and candicidin were recognized (3) as members of a large group of antibiotics, isolated from various *Streptomyces* species. These antibiotics possess in common a high and selective activity against fungi, a general similarity in chemical properties, and a typical three-peaked absorption spectrum revealing the presence within the molecule of a conjugated polyene chromophore containing from four to seven double bonds. A more detailed comparison between candidin and three other members of the group possessing a heptaene chromophore demonstrated (6) that candidin was different, not only from candicidin, but also from ascosin and trichomycin.

A method for the production of candidin in shaken flasks has been described (5). Using stirred tanks, maximum broth activity was attained more rapidly and was considerably higher. The antifungal component was concentrated and the crude solid containing about 50% of candidin was extracted with hot 70% aqueous ethanol to remove the bulk of the impurities. Final purification was achieved by crystallization from a methanol–chloroform–water mixture.

Candidin was obtained as golden-yellow needles which are insoluble in water and most organic solvents. It is relatively soluble in glacial acetic acid, pyridine, and dimethylformamide, and somewhat soluble in many polar solvents such as alcohols, dioxane, or acetone when they are diluted with up to 40% of water. It can be readily dissolved in dilute aqueous mineral acids or sodium hydroxide but not in sodium carbonate. The presence of both basic and acidic groups was confirmed by titration when neutralization equivalents

[1]*Manuscript received May 7, 1956.*
Contribution from the National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan. Issued as Paper No. 226 on the Uses of Plant Products and as N.R.C. No. 4028.

of 928 and 922 were obtained respectively. In acidic solution, candidin is rapidly degraded with loss of the characteristic absorption spectrum, but only a slight loss of activity was detected after four hours in 0.01 *N* sodium hydroxide.

Stable, water-soluble preparations of the antibiotic have been obtained (5, 6) by freeze-drying aqueous solutions at neutral or slightly alkaline pH. Two such fractions, differing in their absorption spectra in neutral aqueous solution, were reported. The less active of these, candidin A, showed a three-peaked spectrum with maxima at 365, 384, and 408 mμ, typical of a conjugated heptaene. The second fraction, candidin B, gave only a single intense absorption maximum at 335–345 mμ. Paper chromatography and counter-current distribution studies have demonstrated, however, that the same antifungal factor is responsible for the activity of the two fractions, and the difference in spectral properties has now been accounted for. Although candidin itself is insoluble in water, neutral freeze-dried preparations containing a mixture of candidin and its sodium salt readily disperse in water to clear "solutions" which are remarkable in possessing only a single intense absorption maximum at 335–345 mμ. If the candidin is brought into true solution, either by adjusting with sodium hydroxide, mineral acid, or by diluting with ethanol, the absorption spectrum reverts to that of a typical conjugated heptaene. The failure of candidin A to show a typical spectral change in neutral aqueous solution was due to the solubilizing action of the large amounts of impurity present in the sample. Lowering the solubility by the addition of sodium chloride was sufficient to effect the conversion to a spectrum showing a single peak of absorption at 335 mμ.

Crystalline candidin does not melt, but darkens slowly above 180° C. Microanalytical data indicate a molecular formula of $C_{46}H_{75}NO_{17}$. No methoxyl or acetyl groups were found, but a Kuhn–Roth determination suggests the presence of six C-methyl groups. Candidin was optically active and gave α_D^{27}° C. = +363° (c = 0.3 in dimethylformamide); +205° (c = 0.3 in glacial acetic acid).

The absorption spectrum in the ultraviolet and visible regions is shown in Fig. 1. Exposure of an alcoholic solution containing catalytic amounts of iodine to strong light does not bring about any change in the wavelengths or intensity of the maxima and it is concluded that the conjugated heptaene is present in the all-*trans* configuration.

The infrared absorption spectrum of candidin is shown in Fig. 2. The strong broad band at 3400 cm.$^{-1}$ together with two intense peaks at 1040 and 1070 cm.$^{-1}$ suggest a polyhydroxy compound, accounting for the high proportion of oxygen in the molecule. The band at 1385 cm.$^{-1}$ can probably be assigned to the C-methyl groups indicated by the Kuhn–Roth determination, while the presence of amino and carboxyl groups is confirmed by the bands at 1555 and 1705 cm.$^{-1}$ respectively. A second band in the carbonyl region at 1715 cm.$^{-1}$ is suggestive of a ketone, but tests with 2,4-dinitrophenylhydrazine, semicarbazide, and Schiff's reagent were negative. Bands at 840, 970, 1015,

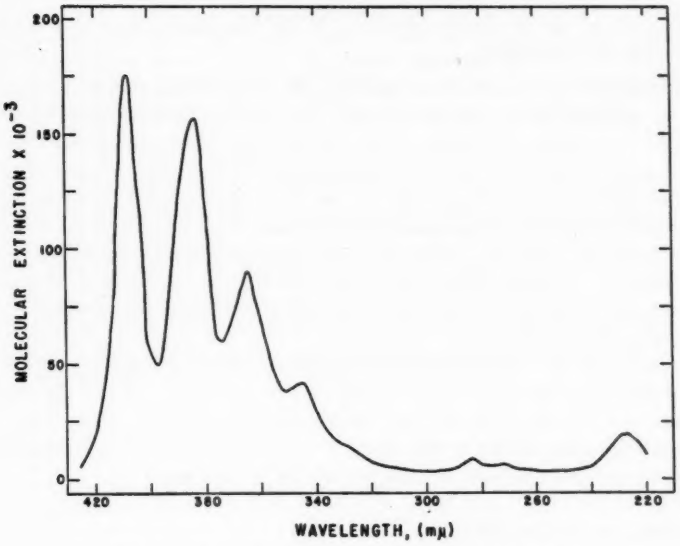

FIG. 1. Absorption spectrum of candidin in ethanol.

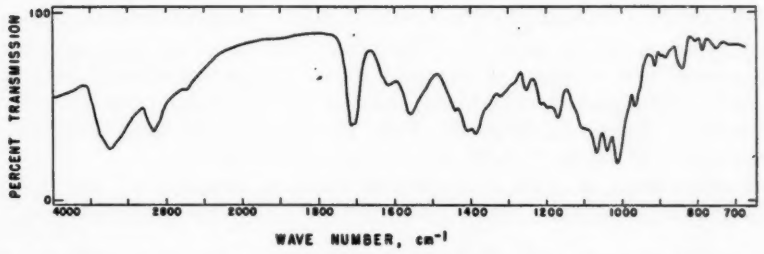

FIG. 2. Infrared absorption spectrum of candidin (pressed potassium bromide pellet).

and 1620 cm.$^{-1}$ are provisionally assigned to the unsaturated groups in the molecule.

Upon hydrogenation under conditions where only carbon to carbon double bonds are reduced, candidin rapidly took up nine moles of hydrogen. The molecule must, therefore, contain two unsaturated groups in addition to the conjugated heptaene chromophore. In view of the absorption maximum in the ultraviolet region at 228 mμ, these are probably present as a conjugated diene.

The antifungal activity of candidin preparations increases with increasing purity. A sample of the crystalline material assayed against *Candida albicans* ATCC 10231 by the cup diffusion method (4) gave a potency of 15,000 units per mgm.

EXPERIMENTAL

Production and Isolation

Candidin was produced on a small scale in a 5 gal. stirred tank. Fifteen liters of medium were inoculated with a shake culture of *S. viridoflavus* as described previously (5) and incubated for four days at 28° C. The whole broth was then adjusted to pH 4.5 with conc. HCl, 2% by weight of filter aid (HyFlo–supercel) stirred in, and the solids separated. They were extracted twice with 10 liters of 70% aqueous ethanol at 50° C., and the extract concentrated under vacuum to 1 liter. The precipitated candidin was separated by centrifugation, washed thoroughly first with 25% aqueous methanol, then with acetone, and dried to yield crude amorphous yellow powder (7.7 gm.) containing 58% candidin.

On a larger scale, candidin was produced in a 150 gal. tank. It was then found more convenient to carry out an initial concentration of the broth to half volume, and dilute with ethanol to a concentration of 70%. The filtered aqueous ethanolic solution was then worked up as described above to give 45 gm. of a crude preparation containing 50% candidin.

Crystallization of Candidin

The crude product (10 gm.) was extracted for 30 min. on a steam bath with hot 75% ethanol (500 cc.). The insoluble residue was extracted by shaking under nitrogen for two hours with a mixture of methanol (1 liter) and chloroform (800 ml.), filtered, and the filtrate diluted with distilled water (400 ml.) and petroleum–ether (400 ml.). The upper layer was separated and slowly evaporated with a stream of nitrogen, when candidin was precipitated as fine needles (600 mgm.). A sample was dried at 25° under phosphorus pentoxide *in vacuo*. Found: C, 60.20; H, 8.24; N, 1.52; *C*—Me, 9.98%. Calc. for $C_{46}H_{75}NO_{17}$: C, 60.44; H, 8.27; N, 1.53; 6*C*—Me, 9.77%.

Further crops of crystalline material could be obtained by repeated extraction of the residual material with the methanol–chloroform mixture.

Neutralization Equivalent

Candidin was titrated as a base in glacial acetic acid with perchloric acid, using crystal violet indicator. The neutralization equivalent was 928.

The acid group in candidin was titrated potentiometrically in dimethylformamide with 0.05 *N* NaOH. The neutralization equivalent was 922. The calculated value for a formula $C_{46}H_{75}NO_{17}$ is 914.

Hydrogenation

Candidin was hydrogenated at atmospheric pressure and room temperature in a microhydrogenation apparatus. Both dimethylformamide and glacial acetic acid were used as solvents, and 5% palladium on carbon, Adams catalyst, and palladium oxide on barium sulphate (1) were used as catalysts. The hydrogenation equivalent was 102 (±5) under all conditions.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to Dr. J. M. Roxburgh and Mr. W. C. Haid for the large scale production of candidin, Mr. J. A. Baignee for the analyses, Miss A. Epp and Mr. M. Mallard for spectral determinations, and Miss D. P. Baker and Mr. F. M. Clare for technical assistance.

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THE SUGAR COMPONENT OF DEOXYRIBONUCLEOSIDES[1]

By I. G. Walker and G. C. Butler

ABSTRACT

From highly polymerized deoxyribonucleate the nucleosides have been isolated by an improved method. The sugar obtained on hydrolysis of the individual nucleosides has been shown to be D-2-deoxyribose in each case.

INTRODUCTION

Although it is assumed that the only carbohydrate constituent of deoxyribonucleate (DNA) is D-2-deoxyribose, the sugar has not been isolated from all of the five nucleosides known to be present in most samples of DNA. Levene and Mori (16) obtained a guanine nucleoside after digestion of calf thymus DNA and concluded that it was a glycoside of D-2-deoxyribose (15). Subsequently other workers found that the same sugar was liberated on acid hydrolysis of the mixed purine deoxynucleosides (6, 10, 12). Similar studies of the pyrimidine deoxynucleosides have been unsuccessful because of the difficulty of cleaving the glycosidic linkages without destroying the sugar.

The results obtained by MacNutt (19) and Friedkin and Roberts (8) in their experiments with nucleoside phosphorylase have provided good evidence that the same sugar is present in the purine—and pyrimidine—deoxynucleosides.

Burke (3) reported, without giving experimental details, that reduction with sodium and ethanol in liquid ammonia rendered pyrimidine nucleosides easily hydrolyzable by Dowex 50 cation exchange resin. The sugars liberated from thymidine and deoxycytidine were identified with D-2-deoxyribose by chromatography and ionophoresis on paper.

In spite of all this evidence we considered that it would be worth while to isolate and to identify in the conventional way the sugar from each of the nucleosides of DNA.

Highly polymerized DNA (20) was hydrolyzed by the combined actions of pancreatic deoxyribonuclease (18) and the phosphodiesterase and 5′-nucleotidase of water moccasin venom. The resulting nucleoside mixture was resolved by anion exchange chromatography (1). Two difficulties were encountered at this stage. The first of these was the finding that the nucleosides of cytosine and 5-methylcytosine did not separate during the chromatography. Therefore, to prepare each of these free of the other the corresponding nucleotides were separated and isolated and from them the nucleosides obtained by hydrolysis with phosphomonoesterase. The second difficulty was that of isolating crystals of the other nucleosides from the large volumes of salt solutions in which they were eluted from the ion exchange column. This problem was solved by our discovery, in common with others (4, 17), that nucleosides and nucleotides were readily adsorbed from aqueous solutions on passage through a column of activated charcoal. When this procedure was applied to the eluates from

[1]*Manuscript received in original form October 25, 1955, and, as revised, June 5, 1956.*
Contribution from the Department of Biochemistry, University of Toronto, Toronto, Ontario.

the ion exchange columns the nucleosides were retained quantitatively on the charcoal column and the salt passed through. The nucleoside (or nucleotide) could be eluted from the charcoal easily with ammoniacal alcohol. Good yields of the nucleosides were obtained and their physical constants agreed well with the most recently reported values (1, 7, 19).

The purine nucleosides deoxyadenosine and deoxyguanosine were most conveniently hydrolyzed by an aqueous suspension of a sulphonic acid cation exchange resin in the hydrogen form (11), the times and temperatures being selected to give a maximum color development when the quantitative Schiff's test (5) was applied to the supernatant solution.

The pyrimidine nucleosides were reduced prior to hydrolysis since Levene and La Forge (13) had demonstrated that ribose could be obtained from uridine by mild acid hydrolysis following catalytic hydrogenation of the nucleoside. Levene and London (14), however, reported that their efforts to hydrogenate thymidine, in the same manner as uridine, were unsuccessful. In our experiments deoxycytidine readily absorbed one mole of hydrogen in the presence of palladium black; the product, on acid hydrolysis, yielded a reducing sugar and dihydrouracil. This was expected since Brown and Johnson (2) had found that cytosine was deaminated on catalytic hydrogenation. Under the same conditions thymidine absorbed two moles of hydrogen and was converted to a substance that did not liberate any reducing or Schiff-positive material on heating with 0.1 *N* or 1.0 *N* sulphuric acid at 100° for periods up to 90 min. This experience made it necessary to use other methods of reducing thymidine, and sodium amalgam was found to be suitable for the purpose. The reduction product in this case was readily amenable to acid hydrolysis.

The hydrolytic conditions needed to free the pyrimidine-bound sugars were harsher than those used for the purine nucleosides. In order to avoid possible chemical changes brought about by this treatment and the preliminary reduction, thymidine and deoxycytidine (after deamination to deoxyuridine) were hydrolyzed with the thymidine phosphorylase system of Friedkin and Roberts (8).

The sugars, liberated by the procedures described above from each of the four nucleosides, were compared with each other and with synthetic L-2-deoxyribose (21) by paper chromatography in two different solvent systems and by the melting points, mixed melting points, and rotations of their crystalline benzylphenylhydrazones. In each of the four cases it was concluded that the sugar was D-2-deoxyribose.

EXPERIMENTAL

All distillations at reduced pressure were carried out with a bath temperature not exceeding 40°.

Isolation and Characterization of the Deoxynucleosides

Twenty grams of DNA, prepared by the method of Marko and Butler (20), was dispersed in 500 ml. of water and hydrolyzed with 150 mgm. of deoxyribonuclease (18). When hydrolysis was complete, the pH of the solution was

adjusted to 9.0 with conc. ammonium hydroxide, and 500 mgm. of lyophilized water moccasin venom,* dissolved in 10 ml. of water, was added. The digest was incubated at 37° and maintained at pH 9.0 by the periodic addition of 2 *N* ammonium hydroxide. When the pH of the digest ceased to fall (4–6 hr.) the addition of ammonium hydroxide was stopped and the digest stored at 37° overnight. After this treatment, analyses usually showed that 70–80% of the total phosphorus of the digest had become inorganic phosphate. In order to carry the release of nucleosides nearer to completion, magnesium formate (equivalent to the phosphate content) was added and the precipitated magnesium ammonium phosphate removed by centrifugation. More of the venom (200 mgm.) was added to the supernatant solution which had been readjusted to pH 9.0, and the mixture was stored at 37° for 15 hr.

The resulting solution was reduced to a volume of 200 ml. by distillation *in vacuo*, brought to pH 10.4 with conc. ammonium hydroxide, and poured onto a column (17 cm. height × 6.8 cm. diameter) of Dowex 2 (200–400 mesh) in the formate form. The flow rate throughout the chromatography was 150 ml. per hr. Each fraction was collected for 30 min. and its nucleoside content measured by ultraviolet spectrophotometry. The procedure and results may be summarized as follows:

Fraction	Nucleoside of	Eluent	Volume (l.)
I	Adenine and cytosine	0.02 *M* formate, pH 9.8	2
II	Thymine	0.05 *M* formate, pH 8.5	2
III	Guanine	0.05 *M* formate, pH 4.5	3

The first of these eluents was prepared by dissolving 0.02 mole of formic acid in 750 ml. of water, adding ammonium hydroxide until the pH was 9.8, adjusting the volume to one liter, and finally readjusting the pH to 9.8 with ammonium hydroxide. The other eluents were prepared by a similar procedure.

After reduction to a volume of 50 ml. by vacuum distillation Fraction I was stored at 5° for 24 hr. Most of the deoxyadenosine crystallized and yields of 1.9–2.0 gm. were obtained. When it was recrystallized from water this material had: nitrogen content, 23.1% (calculated for $C_{10}H_{13}O_3N_5.3H_2O$, 23.0%); m.p. 187.5–189°; $[\alpha]_D^{21}$, −32° (c = 1.11 in water at pH 7.0).

The mother liquors and washings of the deoxyadenosine crystals were combined, adjusted to pH 4.5 with formic acid, and chromatographed on a column of carboxyl cation exchange resin (Amberlite IRC 50, 500 mesh). The column measured 20 cm. in height by 3.4 cm. in diameter and was prepared by washing it with a 0.5 *M* solution of ammonium formate of pH 4.5 followed by water to remove the buffer. After the nucleoside solution had passed into the resin, elution was carried out with 0.05 *M* ammonium formate (pH 4.5) at the rate of 80 ml. per hr. By collecting 60 ml. samples it was found that deoxycytidine was eluted in a volume of 700 ml. followed closely by deoxyadenosine.

**Purchased from Ross Allen's Reptile Institute, Silver Springs, Florida.*

The deoxycytidine solution was passed through a column containing 10 gm. of activated charcoal* and the column washed with 50 ml. of water to remove salt. Elution of the nucleoside from the charcoal was effected with 200 ml. of ammoniacal alcohol (prepared by mixing 500 ml. of 95% ethanol, 430 ml. of water, and 17 ml. of conc. ammonium hydroxide). The resulting filtrate was distilled to dryness under reduced pressure and the residue dried to a fluffy white solid by the repeated vacuum distillation of 10 ml. portions of absolute ethanol. In order to crystallize the deoxycytidine it was converted to the hydrochloride by dissolving the dry residue in 7 ml. of methanol and adding a solution of dry hydrogen chloride in methanol (15 ml. of 3 *N*). Crystallization began almost immediately and after storing at 5° overnight 780 mgm. of crystals were collected. This hydrochloride was recrystallized by dissolving it in 1 ml. of hot water and slowly adding 3 ml. of ethanol. In a melting-point determination the crystals turned brown at 168° and melted with decomposition at 174°. The nitrogen content was 15.8%; calculated for $C_9H_{14}O_4N_3.HCl$, 15.9%. The optical rotation was $[\alpha]_D^{24} = +54.3°$ (in water at pH 7.0, $c = 5.51$ calculated as the free nucleoside).

Fraction II was distilled *in vacuo* to a volume of about 10 ml. On storing this solution at 5°, thymidine crystallized in yields of 1.6 to 2.0 gm. After recrystallization from water the thymidine had: nitrogen content, 10.2% (calculated for $C_{10}H_{14}O_5N_2.2H_2O$, 10.1%); m.p. 189–190°; $[\alpha]_D^{21}$, +18° ($c = 1.16$ in water at pH 7.0).

Fraction III was passed through 15 gm. of charcoal in a column 3.4 cm. in diameter and the column washed with water. Deoxyguanosine was eluted with 1 liter of ammoniacal alcohol. After the volume of the filtrate was reduced to 400 ml. by vacuum distillation and it was stored at 5°, 1.4 gm. of nucleoside crystallized as fine needles. Concentration of the mother liquors yielded another 0.6 gm. After recrystallization from water the deoxyguanosine had: N, 24.3% (calculated for $C_{10}H_{13}O_4N_5.1\frac{1}{4}\ H_2O$, 24.2%); no m.p. up to 250°; $[\alpha]_D^{24}$, −40° ($c = 0.924$ in 0.1 *N* NaOH, pH 12.64).

In order to prepare deoxycytidine free of the 5-methylcytosine nucleoside it was found convenient to dephosphorylate chromatographically pure deoxycytidine-5′-phosphate. Deoxycytidylic acid (310 mgm.) was dissolved in 35 ml. of water and the pH of the solution adjusted to 9.0 with sodium hydroxide. On treatment with 10 mgm. of water moccasin venom for 30 hr. at 38°, all of the phosphorus in the solution had become inorganic. The digest was acidified to pH 5.0 with glacial acetic acid and passed through 3 gm. of charcoal in a column of 2.5 cm. diameter. After the column was washed with 10 ml. of water the nucleoside was eluted with 100 ml. of the ammoniacal ethanol. This eluate was evaporated to dryness and the residue dried by distilling from it 20 ml. portions of absolute ethanol. The residue was dissolved in 5 ml. of methanol and the solution clarified by centrifugation. After 3 ml. of 3 *N* hydrogen chloride in methanol was added to the clear supernatant solution crystals began to appear immediately and 180 mgm. were collected following storage at 5° for a few hours. An additional 35 mgm. of crystals was obtained from the mother

*Darco G–60, Atlas Powder Co.

liquors. The combined product was recrystallized by dissolving it in 0.15 ml. of hot water, slowly adding 2 ml. of absolute ethanol, and chilling. The resulting crystals showed browning at 167° and melted with decomposition at 171°.

When the procedure just described was applied to 110 mgm. of chromatographically pure 5-methyldeoxycytidylic acid, 59 mgm. of 5-methyldeoxycytidine hydrochloride (m.p. 157–158°) was obtained.

Isolation of the Sugar Component of the Purine Deoxynucleosides

Deoxyguanosine (600 mgm.), 2.4 gm. of dry Nalcite HCR*, and 11 ml. of water were mixed in a 15 ml. centrifuge tube and heated at 80° for 10 min. with stirring. The resin was collected by centrifuging and washed three times with small portions of water. Traces of sulphuric acid were removed from the combined supernatant and wash solutions by treatment successively with two drops of 3 *N* barium hydroxide and a small pellet of dry ice. The filtrate obtained from this mixture was concentrated to a sirup *in vacuo* at room temperature.

The sirup was transferred to a 30 ml. beaker with 2 ml. of water and to it were added 300 mgm. of sodium acetate (trihydrate) and 528 mgm. of recrystallized benzylphenylhydrazine hydrochloride dissolved in 4 ml. of β-methoxy-ethanol (methyl cellosolve). The solution was thoroughly mixed and water added to it dropwise with mixing until an opalescence appeared. After storage in the cold the yellow crystals were collected by filtration and washed with methyl cellosolve – water (2 : 1). A final washing with ether removed much of the yellow color leaving 323 mgm. of light yellow needles with m.p. 118–124°. The crude product was purified by dissolving it in the minimum volume of methyl cellosolve, adding two volumes of ether, and storing the solution in the cold. After collection by filtering the white needles that separated melted at 127–128°.

Treatment of deoxyadenosine (600 mgm.) in a similar manner yielded 400 mgm. of crude benzylphenylhydrazone which on recrystallization from methyl cellosolve – ether gave 215 mgm. of white crystals with m.p. 126–128°.

Isolation of the Sugar Component of Deoxycytidine

Deoxycytidine hydrochloride (645 mgm.) was dissolved in 50 ml. of water and the solution neutralized with sodium hydroxide solution. Palladium black (500 mgm.) was added and the hydrogenation allowed to proceed for 3½ hr. at 75° with a hydrogen pressure slightly above atmospheric. The uptake of hydrogen ceased at one mole per mole of nucleoside. After removal of catalyst the solution, now alkaline because of the ammonia released on deamination(2), was neutralized with hydrochloric acid. The nucleoside was adsorbed from the solution by passing it through 9 gm. of charcoal in a column 3.4 cm. in diameter. The column was washed with water to remove salts and the nucleoside eluted with 200 ml. of water: ethanol (1: 1). Solvent was distilled from the eluate, the sirupy residue was dissolved in 20 ml. of 0.1 *N* sulphuric acid, and

**Cation exchange resin converted to the hydrogen form with sulphuric acid, washed with water, and dried in air.*

the solution heated under reflux in a boiling water bath for 30 min. The solution was cooled, neutralized with barium hydroxide, filtered with the aid of a little charcoal, and distilled to dryness *in vacuo*. The residue was dissolved in methanol to give a solution which on slow evaporation deposited crystalline dihydrouracil of m.p. 272° (Lit. (9) 272–274°). From the sugar remaining in the methanol a benzylphenylhydrazone was prepared, two such experiments yielding 180 mgm. of crude product which had m.p. 127–129° after recrystallization from methyl cellosolve – ether.

Isolation of the Sugar Component of Thymidine

Thymidine (400 mgm.) in 10 ml. of water was stirred for two hours with 3 gm. of sodium–mercury amalgam (2.5% sodium). A further 3 gm. of amalgam was added and the stirring continued until all the sodium had reacted. After a further treatment with 3 gm. of fresh amalgam the solution had a low optical density at 2670 Å indicating that reduction of the pyrimidine ring was almost complete. After being filtered the solution was neutralized with 1 *N* sulphuric acid and poured into 10 times its volume of ethanol: ether (4: 1). The precipitated sodium sulphate was removed by filtration and ethanol and ether removed from the filtrate by vacuum distillation. The aqueous solution remaining was adjusted to 20 ml., made $\frac{1}{10}$ *N* with sulphuric acid, and heated at 100° under reflux for 30 min. The sirupy residue left after removal of sulphuric acid and water yielded 135 mgm. of crude benzylphenylhydrazone which on recrystallization from methyl cellosolve – ether had m.p. 127–129°. No dihydrothymine was isolated in these preparations and subsequent experiments showed that it was destroyed in alkaline solution.

Enzymatic Hydrolysis of Deoxycytidine and Thymidine

The enzyme thymidine phosphorylase was extracted from fresh rat liver as described by Friedkin and Roberts (8) but the purification was not carried beyond the first fractionation with ammonium sulphate.

Thymidine (1.8 mM.) was dissolved in 50 ml. of 0.1 *M* arsenate – 0.1 *M* succinate buffer of pH 5.9 and added to 100 ml. of enzyme solution. After incubation of the mixture at 38° for 16 hr. spectrophotometric assay (8) indicated complete arsenolysis of the nucleoside. A protein precipitate was removed by centrifugation and the remainder of the protein in solution was precipitated by the addition of one-tenth volume of 3% perchloric acid and centrifuging. The combined supernatant solution and water washings of the precipitate were reduced to a volume of 50 ml. by vacuum distillation and desalted by passage in turn through a 50 cc. bed of Nalcite HCR (H form) and 50 cc. of Dowex 1 (Acetate form). The dry residue, obtained from the effluent solution by distillation, was converted to the benzylphenylhydrazone in the usual manner. The recrystallized product weighed 140 mgm. and had m.p. 126–128°.

Thymidine phosphorylase acts upon thymidine and deoxyuridine but not upon deoxycytidine. Consequently, to obtain the sugar from this last nucleoside it was deaminated by the method of MacNutt (19) before treatment with the enzyme. Thus 1.6 mM. of deoxyuridine yielded 83 mgm. of recrystallized sugar benzylphenylhydrazone with m.p. 126–128°.

Specific Rotations of the Benzylphenylhydrazones

The optical rotations of the benzylphenylhydrazones, prepared as described in the foregoing, were measured in pyridine solution and compared with that of the same derivative of synthetic L-2-deoxyribose (21) which derivative had m.p. 126–128°. The results are to be found in Table I.

TABLE I

A COMPARISON OF THE OPTICAL ROTATIONS OF THE BENZYLPHENYLHYDRAZONES DERIVED FROM THE DEOXYNUCLEOSIDE SUGARS AND SYNTHETIC L-2-DEOXYRIBOSE

Benzylphenylhydrazone derived from	Method of preparation of sugar	Specific rotation in pyridine		
		Temp. (°C.)	Concn. (%)	$[\alpha]_D^t$
Deoxyguanosine	Resin hydrolysis	20	3.5	−19°
Deoxyguanosine	Resin hydrolysis	18	3.0	−18°
Deoxyguanosine	Resin hydrolysis	23	2.5	−16°
Deoxyadenosine	Resin hydrolysis	24	4.2	−20°
Deoxyadenosine	Resin hydrolysis	20	3.5	−17°
Deoxycytidine	Catalytic hydrogenation and acid hydrolysis	27	4.6	−17°
Deoxycytidine	Enzymatic hydrolysis	28	4.2	−16°
Thymidine	Amalgam reduction and acid hydrolysis	24	4.7	−19°
Thymidine	Amalgam reduction and acid hydrolysis	20	2.3	−15°
Thymidine	Enzymatic hydrolysis	25	5.4	−18°
Synthetic L-2-deoxyribose		18	4.0	+21°
Synthetic L-2-deoxyribose		21	3.0	+20°

Comparison of Sugars by Paper Chromatography

Two solvent systems were used: (*a*) butanol, pyridine, water, 8:2:1, and (*b*) butanol, ethanol, water, 4:1:1. Chromatograms on Whatman No. 3 paper were developed upwards until the solvent front had reached a height of 15 cm. This needed 1.5 hr. for system (*a*) and 2 hr. for system (*b*). After development the papers were dried in a warm oven, sprayed with a 2% solution of *m*-phenylenediamine hydrochloride in 75% ethanol (6), and heated at 100° for 5 min. The positions of the sugars were indicated by spots fluorescing under ultraviolet light.

The following sugars were compared by simultaneous chromatography:

1. Two samples obtained from the hot acid (resin) hydrolysis of deoxyadenosine and deoxyguanosine.
2. Two samples from the enzymatic arsenolysis of thymidine and deoxyuridine.
3. One sample from the hot acid hydrolysis of reduced thymidine.
4. Glucose.
5. Arabinose.
6. L-2-Deoxyribose.

The R_f values so obtained were:

With system (*a*): All nucleoside sugars and L-2-deoxyribose, 0.43; glucose, 0.14; arabinose, 0.22.

With system (*b*): All nucleoside sugars and L-2-deoxyribose, 0.43; glucose, 0.23; arabinose, 0.34.

ACKNOWLEDGMENTS

Financial support of this work was provided by the Kate E. Taylor fund of the Banting Research Foundation and by the National Research Council of Canada.

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THE LIMITING HEAT OF SOLUTION OF PLUTONIUM IN SOME RARE EARTH METALS[1]

By D. E. McKenzie, W. M. Jenkinson, and A. S. Denovan

ABSTRACT

The distribution of plutonium between neutron-irradiated uranium and some rare earth metals has been examined as a function of temperature in the range 1160° to 1350°C. The results are used to calculate $\bar{L}°_{Pu}$, the limiting partial molal heat content of plutonium, at 1250°C. in lanthanum, cerium, neodymium, and a commercial preparation of mixed rare earths (misch metal). The following values (in kilocalories) were obtained: lanthanum 2.9, cerium 1.1, neodymium 0.0, and misch metal 1.1. The maximum error associated with these values is ±0.4 kilocalories.

INTRODUCTION

In a previous paper (2) the limiting heat of solution of plutonium in liquid silver was determined. The method consisted of measuring the effect of temperature on the distribution of plutonium between neutron-irradiated uranium and silver. Similar measurements have been made during a study of the distribution of plutonium between uranium fuel and some rare earth metals. The data on plutonium distribution as a function of temperature have been used to calculate values for the heat of solution of plutonium in lanthanum, cerium, neodymium, and a commercial preparation of mixed rare earths (misch metal). The results are presented in this paper. Experiments in which lanthanum and cerium were used as extractants for plutonium have been reported by Spedding and co-workers of the Ames laboratory of the United States Atomic Energy Commission (5).

EXPERIMENTAL

Materials and Apparatus

The neutron-irradiated uranium was cut from rods which had been irradiated in the NRX reactor and allowed to decay for three years. The concentration of plutonium in this material was 0.025%. The purities of the lanthanum, cerium, and neodymium, which were obtained from A. D. MacKay, Inc. as metal billets, are given in Table I. Table I lists, also, the materials other than rare earths in the misch metal (New Process Metals Inc.). The approximate

TABLE I

ANALYSES OF EXTRACTANTS

Extractant	Major component	Impurities
Lanthanum	97–98% La	Other rare earth metals
Cerium	98.6% Ce	Other rare earth metals
Neodymium	99% Nd	Other rare earth metals
Misch metal	98% rare earths	1.32% Fe, 0.58% Mg, 0.09% silica

[1]*Manuscript received May 16, 1956.*
Contribution from the Research Chemistry Branch, Atomic Energy of Canada Limited, Chalk River, Ontario. Issued as A E C.L. No. 337.

percentages of the rare earths in this preparation are as follows: cerium 50–55%, lanthanum 20–25%, neodymium 15–20%, praseodymium 5–7%, and other rare earth metals 2–5%.

The metals were contacted in beryllia or alumina crucibles. The beryllia crucibles were obtained from the Atomic Energy Research Establishment, Harwell, England; the alumina crucibles ('Triangle' recrystallized alumina) were obtained from The Morgan Crucible Co. Ltd.

The uranium and rare earth metal were heated by a tungsten wire coil surrounded by thermal and radiation shields. The assembly was mounted in a glass bulb which could be evacuated by diffusion and mechanical pumps.

Temperatures were measured with a platinum, platinum 10% rhodium thermocouple which was coiled in the heating zone as a seat for the crucible containing the charge. The thermocouple was calibrated to give the temperature of the charge by melting various pure metals, in the appropriate crucible, in the apparatus. The calibration was checked frequently, generally after three runs. The temperatures are considered to be accurate to $\pm 5°$ C.

Procedure

For an experiment, weighed amounts of neutron-irradiated uranium and a rare earth metal in the oxide crucible were placed in the apparatus. The uranium had been etched in acid to remove approximately 25% of its weight for a reference solution, then washed in water and acetone. The glass bulb was pumped down to a pressure of 10^{-5} mm. of Hg or less before admitting welding grade argon to a pressure of one atmosphere. The charge was then heated to temperature and held for 20 min., which was found to be ample time to establish equilibrium.

After equilibration the melt was essentially quenched by shutting off the power since the uranium phase solidified in about 15 sec. even for experiments at the highest temperatures. The metal billet, after further cooling in argon, was removed from the crucible and the two phases separated mechanically. In all cases the complete phase, after weighing, was dissolved for analyses.

Analyses

The phases were analyzed for plutonium by the direct counting of thin sources prepared from the solutions. For each run at least two determinations, on separate days, were made of the ratio of α counts due to plutonium in the two phases. This ratio was checked for some experiments by analyzing for plutonium using the LaF_3 procedure.

The distribution coefficient for plutonium, K_{Pu}, was calculated from the expression

$$K_{Pu} = \frac{\text{Pu counts in rare earth}}{\text{Pu counts in uranium}} \times \frac{\text{moles of uranium}}{\text{moles of rare earth}} .$$

There is negligible error in assuming that this K_{Pu} is the ratio of the mole fraction of Pu in rare earth to the mole fraction of Pu in uranium. In making these calculations for the misch metal runs the atomic weight of cerium was used to calculate the number of moles of misch metal.

RESULTS AND DISCUSSION

The results are summarized in Table II. The runs in which lanthanum or neodymium was the extractant were made using beryllia crucibles. The first two cerium runs were performed in beryllia crucibles but alumina was used for the remainder. Liquid cerium at temperatures above 1200° C. appeared to wet and seep through the beryllia crucibles. All experiments with misch metal were carried out in alumina containers.

Plutonium distributions at 1200° C. have been obtained for the systems La–U and Ce–U at the Ames laboratory (5). In the Ames work two different

TABLE II

DATA FOR THE DISTRIBUTION OF PLUTONIUM
Initial Pu concn. = 0.025%

Extractant	Temp. (°C.)	Wt. U (gm.)	Wt. ext. (gm.)	Pu ratio* (ext./U)	K_{Pu}
La	1160	3.8553	4.5516	0.682	0.337
	1170	4.2390	4.3000	0.600	0.345
	1205	4.0230	4.0806	0.608	0.350
	1243	4.0485	4.4262	0.669	0.357
	1276	3.7839	3.7946	0.629	0.366
	1310	3.9280	4.0400	0.661	0.375
	1325	4.3172	4.8266	0.721	0.376
Ce	1160	3.4927	3.4463	0.892	0.532
	1200	4.0471	4.0823	0.917	0.535
	1250	3.9108	4.3846	1.035	0.543
	1300	4.5153	4.7902	0.993	0.551
	1330	3.8892	4.2914	1.031	0.550
	1350	3.7774	3.9650	0.995	0.558
Nd	1160	4.0560	4.6804	0.936	0.491
	1200	3.8435	4.0958	0.853	0.484
	1250	4.0620	4.1406	0.822	0.488
	1250	4.1038	4.0768	0.798	0.486
	1300	4.5446	4.8170	0.858	0.490
	1300	4.0840	4.1413	0.818	0.488
	1350	3.9100	3.8994	0.803	0.487
Misch metal	1160	3.9115	4.1663	0.807	0.446
	1200	3.8281	3.9717	0.790	0.448
	1250	4.3880	4.4115	0.775	0.454
	1300	4.3491	4.2841	0.768	0.459
	1350	4.1323	3.9633	0.756	0.464
	1350	4.2680	4.5114	0.837	0.466

**Average of at least two determinations.*

TABLE III

COMPARISON OF PLUTONIUM DISTRIBUTIONS AT 1200°C. FOR THE SYSTEMS La–U AND Ce–U

Extractant	Initial Pu conc. in U (%)	K_{Pu}	
		Ames (5)	Chalk River
La	0.023	0.326	0.350
	0.0018	0.379*	
Ce	0.023	0.600	0.535
	0.0018	0.559	

**Average of two runs*

samples of uranium, of plutonium concentrations 0.023% (i.e. the same as in this study) and 0.0018%, were used. The results are compared with those of this work in Table III.

The distribution data are plotted as log K_{Pu} vs. $1/T$ in Fig. 1. The straight lines of Fig. 1 were obtained from a least squares treatment of the data which yielded the following equations:

Lanthanum, $\log K_{Pu} = -0.0302 - 629/T$;
Cerium, $\log K_{Pu} = -0.105 - 243/T$;
Neodymium, $\log K_{Pu} = -0.315 + 5.3/T$;
Misch metal, $\log K_{Pu} = -0.190 - 232/T$.

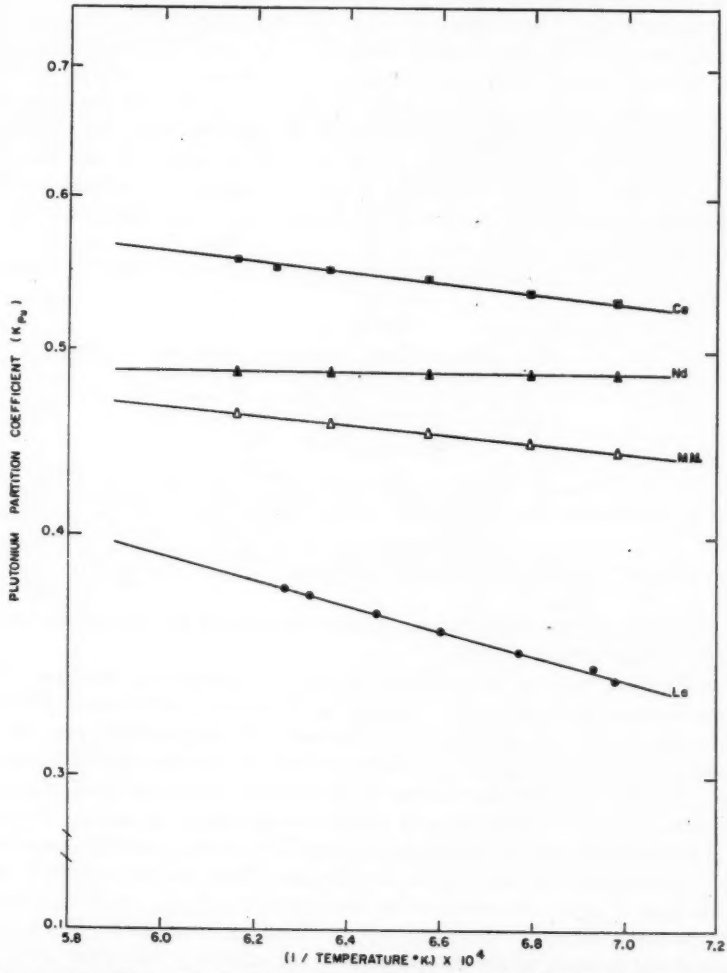

FIG. 1. The effect of temperature on the distribution of plutonium between neutron-irradiated uranium and some rare earth metals. Uranium/rare earth weight ratio = 1/1. Initial concentration of plutonium in uranium = 0.025%.

The slope of any one of these lines (e.g. lanthanum) can be related to the heat effect associated with the transfer of one gram-atom of plutonium from neutron-irradiated uranium to lanthanum, or, the sum of a total or integral heat of solution of plutonium in lanthanum and a heat of dilution of plutonium in uranium, i.e.

$$\Delta H_{tr} = \underset{\text{Pu in La}}{\Delta H_S} + \underset{\text{Pu in U}}{\Delta H_D}$$

Independent measurements of the volatilization of plutonium from metallic uranium fuel (1, 3) provide evidence that, for low concentrations in the temperature range 1540–1770° C., plutonium in neutron-irradiated uranium behaves essentially as an ideal solution. If this conclusion is accepted and, also, the assumption made that ideality extends to the lower temperatures of this work, then the heat of dilution of plutonium in uranium is zero. The measured heat of transfer, therefore, gives directly a total heat of solution, per gram-atom of plutonium, of liquid plutonium in liquid lanthanum. Also, since the equilibrium plutonium concentrations in the extractant metal are less than 0.01 atomic per cent, the heat of transfer is the limiting heat of solution or $\bar{L}^\circ_{Pu}$, the limiting partial molal heat content, relative to liquid plutonium, of plutonium in liquid lanthanum (4).

The values of $\bar{L}^\circ_{Pu}$ obtained from the present work are listed in Table IV.

TABLE IV

THE LIMITING PARTIAL MOLAL HEAT CONTENT OF PLUTONIUM IN SOME RARE EARTH METALS AT 1250°C.

Metal	$\bar{L}^\circ_{Pu}$ (kcal.)
Lanthanum	2.9±0.4
Cerium	1.1±0.4
Neodymium	0.0±0.4
Misch metal	1.1±0.4

The listed error in the heat content is that introduced by the uncertainties in a single determination of K_{Pu}.

The limiting heat of solution of plutonium appears to decrease as the atomic number increases in the "cerium" group of rare earth metals. The value of $\bar{L}^\circ_{Pu}$ decreases from lanthanum to cerium and is essentially zero for neodymium. It is interesting to note that neodymium occupies, in the lanthanide series, the same position as uranium in the actinide series and both exhibit the same limiting heat of solution with respect to plutonium as solute. The misch metal preparation used in this study is about 50% cerium and possesses a value of $\bar{L}^\circ_{Pu}$ essentially the same as that of cerium. Since the extractant is mixed in this case it is not necessary that the variation of K_{Pu} with temperature satisfy a single equation (because, say, of changing composition due to distillation of one or more of the components of the mixture). However, within the precision of the data, a straight line is obtained. Thus the addition of the other

rare earths to cerium decreases the amount of plutonium distributed to the cerium phase but does not affect the limiting heat of solution of plutonium in the phase.

The distribution of fission product cerium has been determined in some of the experiments. In this connection it has been reported that the solubility of cerium in uranium is 1.2% at 1150° C. and may increase considerably with temperature (5). If it is assumed that all the rare earths employed in this study are equivalent in their behavior toward one another and, also, in their behavior toward uranium then, at 1150° C., 98.8% of the fission product cerium should be found in the rare earth phase and 1.2% in the uranium phase. The experimental results, which are collected in Table V, show reasonable agreement with this conclusion and provide support that equilibrium was established in the experiments.

TABLE V

DISTRIBUTION OF FISSION PRODUCT CERIUM BETWEEN URANIUM AND SOME RARE EARTH METALS

Extractant	Temp. (°C.)	Fission product Ce distribution (% original)		
		Extractant	Uranium	Crucible
Lanthanum	1160	90.8	2.1	1.6
	1276	97.5	1.4	2.8
Cerium	1200	99.6	0.0	1.9
	1250	96.0	3.2	0.3
Neodymium	1200	89.7	2.2	0.4
	1300	98.4	1.6	1.2

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L-SERYLGLYCYLGLYCINE[1]

By Erich Baer, Jonas Maurukas,[2] and Donald D. Clarke

ABSTRACT

A synthesis of the hitherto unreported L-serylglycylglycine by two different methods is described. N-carbobenzoxy L-serylglycylglycine benzyl ester, an intermediate in the preparation of the tripeptide, was found to be a suitable derivative in the synthesis of L-α-phosphatidyl L-serylglycylglycine.

In previous publications from this laboratory (1–9) methods for the synthesis of choline, ethanolamine, and serine-containing glycerolphosphatides have been described. A comparison of the synthetic and naturally occurring phosphatides led to an unambiguous elucidation of the structure and configuration of several naturally occurring lecithins, cephalins, and phosphatidyl serine. The recent discovery of naturally occurring phosphatides with peptides as nitrogenous moieties (10, 11, 18, 21, 24) challenged us to attempt the synthesis of a phosphatidyl peptide. Obviously, the difficulty of preparing peptides of even moderate chain length made it imperative that in the beginning we restrict ourselves to the synthesis of a phosphatidyl peptide with a relatively simple peptide moiety. L-Serylglycylglycine was chosen as it was expected that its preparation would not offer too many difficulties and that the phosphatidyl tripeptide would exhibit some of the properties of natural phosphatidyl peptides. Serylglycylglycine, however, is not a suitable compound for phosphorylation because of the presence of a free amino and carboxyl group. Hence, the N-carbobenzoxy L-serylglycylglycine benzyl ester, in which both groups are blocked by readily removable substituents and which is a precursor in the synthesis of the tripeptide, was used. This paper describes the synthesis of L-serylglycylglycine, a tripeptide not previously reported.

The specific rotation of L-serylglycylglycine ($[\alpha]_D^{25°}$ +32.5°) was found to be higher than that of L-serylglycine ($[\alpha]_D^{25°}$ +30.5°) reported by Fruton (19) although by analogy with peptides of a similar constitution (20) the addition of a glycine moiety to L-serylglycine should have resulted in a lower rotation. Hence L-serylglycylglycine was synthesized by a second procedure. The specific rotation of the tripeptide again was found to be +32.5°. Repeated checks bore out the correctness of this value. In addition the optical activity of L-serylglycylglycine was measured at various temperatures within the range of 11°–50°. The results are recorded in Table I.

[1]*Manuscript received May 31, 1956.*

Contribution from the Banting and Best Department of Medical Research, University of Toronto, Toronto, Ontario. Supported by a Research Grant of the National Research Council of Canada, Division of Medical Research, Ottawa, Canada. An account of the work described in this paper was presented at the Symposium on Phospholipids at the University of Western Ontario, London, Ontario, Canada, October 12–13, 1955.

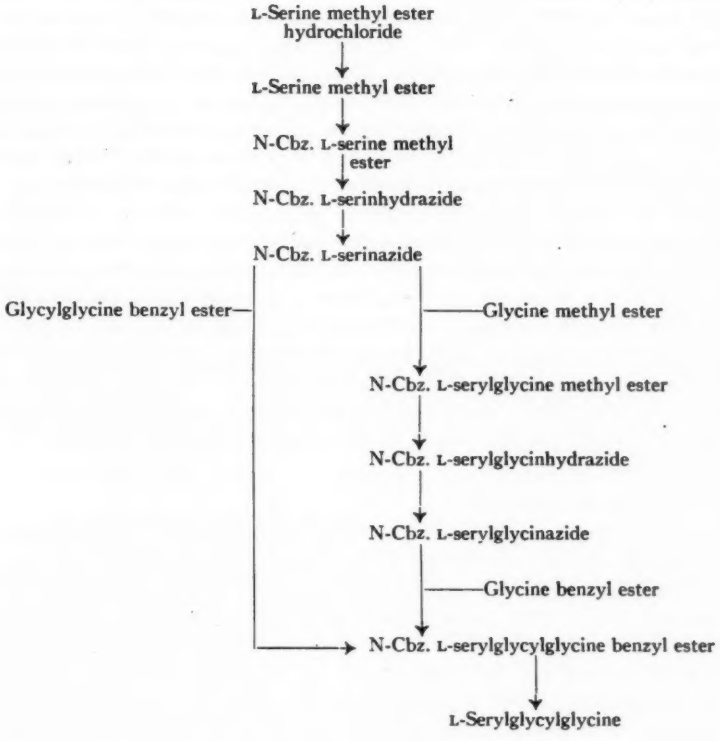
[2]*A section of this paper forms part of a thesis submitted by Jonas Maurukas to the Department of Pathological Chemistry of the University of Toronto in partial fulfillment of the requirements for the degree of Doctor of Philosophy.*

TABLE I

OPTICAL ROTATION OF L-SERYLGLYCYLGLYCINE AT VARIOUS TEMPERATURES

Temp. (°C.)	$[\alpha]_D$*
11	+35.4
17	+34.1
25	+32.5
30	+32.2
33	+31.6
45	+29.7
50	+28.6

Concentration: 5.4% in 1 N HCl.



Cbz. = carbobenzoxy

REACTION SCHEME

EXPERIMENTAL

N-Carbobenzoxy L-Serylglycylglycine Benzyl Ester

Procedure I

N-Carbobenzoxy L-Serinhydrazide

A synthesis of N-carbobenzoxy L-serinhydrazide *via* the N-carbobenzoxy L-serine methyl ester hydrochloride has been reported by Fruton (19). Since his description is rather brief, the procedure is reported in greater detail here. *N-carbobenzoxy L-serine methyl ester*: In a 500 ml. two-necked round-bottomed flask equipped with a motor-driven stirrer were placed 100 ml. of water, 48 gm. of sodium bicarbonate, 75 ml. of ether, and 13.2 gm. of L-serine methyl ester hydrochloride (17). The flask was immersed in an ice-cold water bath and 10 min. later 21.0 ml. of freshly prepared carbobenzoxy chloride was added in the course of 20 min., while stirring vigorously. After two hours the bath was removed and the stirring was continued for an additional 30 min. The ether and water layers were separated, and the water layer was washed with two 35 ml. portions of ether. The combined ether solutions were freed from carbobenzoxy chloride by the addition of pyridine in just sufficient amounts to destroy the unreacted portion of the chloride, and then were washed successively with water, 2.5 *N* hydrochloric acid, and water. Drying the ether solution with anhydrous sodium sulphate and subsequent evaporation of the solvent under diminished pressure yielded N-carbobenzoxy L-serine methyl ester. (This compound was also obtained in a good yield by methylating N-carbobenzoxy L-serine (7) with diazomethane.) *Hydrazide*: The N-carbobenzoxy L-serine methyl ester, without further purification, was dissolved in 100 ml. of 99% ethanol, and to its solution was added 4.7 ml. of hydrazine hydrate. The N-carbobenzoxy L-serinhydrazide began to crystallize almost immediately. After it had been left at room temperature for 10 hr., the mixture was filtered with suction, the hydrazide was washed with cold 99% alcohol followed by ether and dried *in vacuo*. Obtained were 13 gm. of N-carbobenzoxy L-serinhydrazide (54% of the theory based on serine), m.p. 181°. Reported by Fruton (19), m.p. 181°.

N-Carbobenzoxy L-Serinazide

To a cold (−5°) and vigorously stirred solution of 13 gm. of N-carbobenzoxy L-serinhydrazide in a mixture of 60 ml. of glacial acetic acid and 223 ml. of 0.5 *N* hydrochloric acid was added a concentrated aqueous solution of 3.9 gm. of sodium nitrite. The azide formed immediately and precipitated as an oil. Crystallization of the azide was induced by mechanical means and the crystals were washed with ice-cold water. The dry and crystalline N-carbobenzoxy L-serinazide, which weighed 10.4 gm., and which appeared to be quite stable at room temperature, melted from 61° to 63° with the evolution of gas. On further heating the melt solidified to melt again at 169°–171°.

The higher melting substance evidently is 4-carbobenzoxyaminooxazolidone-2 (m.p. 171°), which was obtained by Fruton (19) by rearrangement of N-carbobenzoxy L-serinazide in ethyl acetate solution at 40°. When Fruton's

procedure was repeated, 4-carbobenzoxyaminooxazolidone-2, m.p. 169°–171°, with a specific rotation of $[\alpha]_D^{25}$ −50° in ethyl acetate (*c*, 0.6), was obtained. The retention of optical activity on rearrangement is in agreement with the mechanism suggested by Kenyon and Young (22) for the Curtius rearrangement.

Glycylglycine Benzyl Ester Hydrochloride

Glycylglycine (14.4 gm.) was converted to its benzyl ester benzenesulphonate as described by Miller and Waelsch for glycine (23); 39 gm. (95%) of crude product was obtained. This material was added to 325 ml. of 99% ethanol, and dry hydrogen chloride gas was passed into the mixture with swirling until a clear solution resulted. After a few minutes crystallization set in. The mixture was cooled in an ice bath, filtered with suction, and the precipitate was washed with cold 99% ethanol followed by dry ether. On recrystallization of the crude product (15.2 gm.) from 200 ml. of hot 99% ethanol, 13.0 gm. of glycylglycine benzyl ester hydrochloride (50%) was obtained, m.p. 159°–161°C.

Glycylglycine benzyl ester hydrochloride was also prepared according to the procedure of Cook *et al.* (13, 14) for the synthesis of glycyl peptides, by coupling 2-thio-5-thiazolidone with glycine benzyl ester. The chloroform which was used by these authors was replaced by dichloromethane as this solvent facilitated the crystallization of the benzyl ester hydrochloride, m.p. 159°–160°C.

Neither of these preparations gave melting point depressions with glycylglycine benzyl ester hydrochloride prepared by the method of Zervas and Theodoropoulos (26).

Glycylglycine Benzyl Ester

Glycylglycine benzyl ester hydrochloride (13.0 gm.) suspended in 130 ml. of dry chloroform was treated with dry ammonia gas in excess and the fine precipitate of ammonium chloride was removed by filtration. The solvent was distilled off under reduced pressure to remove excess ammonia, and the glycylglycine benzyl ester was redissolved in 100 ml. of chloroform.

N-Carbobenzoxy L-*Serylglycylglycine Benzyl Ester*

The solution of glycylglycine benzyl ester in chloroform, obtained in the previous step, was added to a solution of 10.4 gm. of N-carbobenzoxy L-serinazide in 200 ml. of dry ether. A precipitate was formed immediately. The mixture, after having been kept overnight at room temperature, was cooled to −10°, filtered with suction, and the solid was washed first with dry chloroform and then with dry ether. The crude material, weighing 18 gm., on recrystallization from 100 ml. of 99% ethanol yielded 13 gm. of N-carbobenzoxy L-serylglycylglycine benzyl ester (58% based on N-carbobenzoxy L-serinhydrazide), m.p. 150°–152°. A further recrystallization from ethanol yielded a material melting from 151° to 153°. Anal. Calc. for $C_{22}H_{25}O_7N_3$ (443.45): C, 59.58; H, 5.68; N, 9.48. Found: C, 59.11; H, 5.62; N, 9.50

Procedure II

Glycine Methyl Ester

The ester was prepared from glycine methyl ester hydrochloride by the procedure of Curtius and Goebel (15), except that a small and controlled amount of water was added to ensure a rapid reaction. The modified procedure is as follows.

A mixture of 14 gm. (111.5 mM.) of finely powdered glycine methyl ester hydrochloride, 12.9 gm. (55.7 mM.) of finely powdered silver oxide, and 85 ml. of anhydrous ether, to which 15 drops of distilled water had been added, was vigorously shaken for three hours. At the end of this period the ether was decanted and the residue was washed with three 20 ml. portions of anhydrous ether. The combined ether solutions, which contained approximately 70% of the theoretical amount of the glycine methyl ester, were dried with barium oxide. The glycine methyl ester is sufficiently stable in ether solution that, if necessary, it can be stored in this form for several days without suffering decomposition.

N-Carbobenzoxy L-*Serylglycine Methyl Ester*

This substance was prepared from N-carbobenzoxy L-serinazide and glycine methyl ester following Erlanger and Brand's procedure for the preparation of substituted glycine and alanine dipeptides (16). A dry and ice-cold solution of N-carbobenzoxy L-serinazide prepared as described above from 13.0 gm. of N-carbobenzoxy L-serinhydrazide was added to an ether solution of glycine methyl ester obtained from 14 gm. of glycine methyl ester hydrochloride. The formation of the N-carbobenzoxy L-serylglycine methyl ester took place rapidly; most of it precipitated during the first 10 min. After it had been standing for 20 hr. at room temperature and one hour at $-10°$, the mixture was filtered by suction, the solid was washed with cold ether and dried *in vacuo* over sodium hydroxide. The crude material, weighing 14 gm., on re-precipitation from 75 ml. of warm ethyl acetate by the addition of low-boiling petroleum ether, yielded 12.5 gm. (78.5%) of crystalline N-carbobenzoxy L-serylglycine methyl ester, m.p. 100–101°. Anal. Calc. for $C_{14}H_{18}O_6N_2$ (310.3): N, 9.03. Found: N, 9.20.

N-Carbobenzoxy L-*Serylglycinhydrazide*

The hydrazide was prepared as follows (12, 16): A solution of 11.2 gm. of N-carbobenzoxy L-serylglycine methyl ester and 4.5 ml. of hydrazine hydrate in 100 ml. of 99% ethanol was refluxed for one hour. During this time most of the hydrazide precipitated as a crystalline mass. After it had been left for 12 hr. at room temperature, the mixture was filtered by suction, the hydrazide was washed with cold 99% ethanol, followed by ether, and was dried *in vacuo* over sodium hydroxide. Yield 9.4 gm. (83.9% of theory); m.p. 186°–187°, reported m.p. 181°–182° (20). This substance is relatively stable and can be stored, if necessary, for future use. Anal. Calc. for $C_{13}H_{18}O_5N_4$ (310.31): N, 18.05. Found: N, 17.74.

N-Carbobenzoxy L-*Serylglycylglycine Benzyl Ester*

Azide: To a clear solution of 9.5 gm. (30.6 mM.) of N-carbobenzoxy L-serylglycinhydrazide in 65 ml. of glacial acetic acid and 325 ml. of 0.5 *N* hydrochloric acid was added with shaking a concentrated aqueous solution of 2.1 gm. (31.0 mM.) of sodium nitrite, and the mixture was cooled to −5°. The N-carbobenzoxy L-serylglycinazide was extracted with two 250 ml. portions of an ice-cold mixture of ether – ethyl acetate (1:1, v/v). The combined extracts were washed with a cold and concentrated aqueous solution of bicarbonate until the washings remained alkaline to red litmus paper. The cold solution of the azide, after being dried briefly with anhydrous sodium sulphate, was added to the dry ethereal solution of glycine benzyl ester that had been prepared from 9.2 gm. of glycine benzyl ester hydrochloride by the procedure of Miller and Waelsch (23). After the solution had been left for six hours at room temperature and one hour at 0°, the crystalline material was filtered off, washed with ether, and dried over sodium hydroxide *in vacuo*. The crude product (9.5 gm.) on reprecipitation from a solution in 10 ml. of 99% ethanol by the gradual addition of ether yielded 8.5 gm. of N-carbobenzoxy L-serylglycylglycine benzyl ester (62.7% based on N-carbobenzoxy L-serylglycinhydrazide), m.p. 151°–153°.

TRIPEPTIDE

L-Serylglycylglycine

Two grams of N-carbobenzoxy L-serylglycylglycine benzyl ester, prepared by either one of the above procedures, was dissolved in 60 ml. of 80% acetic acid (12), and to the solution was added 0.2 gm. of palladium black (25). The mixture was shaken vigorously at room temperature in an atmosphere of pure hydrogen at an initial pressure of approximately 50 cm. of water until the consumption of hydrogen had ceased completely. The hydrogen was replaced by nitrogen, the catalyst was filtered off, and both hydrogenation vessel and catalyst were washed with distilled water. The combined filtrate and washings were evaporated to dryness under reduced pressure (bath 35°–40°). The residue was dissolved in 10 ml. of water and to the solution was added with stirring 20 ml. of 99% ethanol. After cooling to −10°, the mixture was filtered with suction and the precipitate was washed with dry ethanol. The L-serylglycylglycine, which frequently was obtained in the form of a monohydrate, after being dried *in vacuo* at 120°, weighed 0.9 gm. (91% of theory). The tripeptide, obtained from N-carbobenzoxy L-serylglycylglycine benzyl ester prepared either by procedure I or II, melted with decomposition at 216° (the capillary was placed in an oil bath at 200° and the temperature of the bath was raised 10° per min.) and had a specific rotation $[\alpha]_D^{25}$ +32.5° in 1 *N* hydrochloric acid (*c*, 5.4). Anal. Calc. for $C_7H_{13}O_5N_3$ (219.2): C, 38.35; H, 5.98; N. 19.17. Found: C, 38.24; H, 5.74; N, 18.83 (Dumas).

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LYCOPODIUM ALKALOIDS

III. FUNCTIONAL GROUPS OF SOME MINOR ALKALOIDS OF L. ANNOTINUM[1]

By G. S. Perry[2] and David B. MacLean

ABSTRACT

Four minor alkaloids of *L. annotinum* have been examined by chemical methods and infrared spectroscopy for their functional groups. Acrifoline (L.27) $C_{16}H_{23}O_2N$ has a double bond, a carbonyl group, and an hydroxyl function. Annotine (L.11) $C_{16}H_{21}O_3N$ has a double bond, a carbonyl group, an hydroxyl function, and an inert oxygen probably present in an ether linkage. Alkaloid L.12 ($C_{18}H_{25}O_3N$) is *O*-acetylacrifoline. Alkaloid L.8 ($C_{16}H_{25}O_2N$) has only been studied by infrared spectroscopy where it shows carbonyl and hydroxyl absorption. All four alkaloids therefore contain a basic tetracyclic ring system as do the majority of other lycopodium alkaloids. Annotoxine, a molecular compound of acrifoline and annotine, has been isolated from extracts of Canadian plant material.

The first detailed examination of the alkaloids of *Lycopodium annotinum* L. was carried out by Manske and Marion (6) on plant material of Canadian origin. In 1952, Bertho and Stoll (4) examined *L. annotinum* L. of German origin, and more recently Achmatowicz and Rodewald (1) have intensively investigated the *L. annotinum* L. native to Poland. The work of Bertho and Stoll indicated that the alkaloidal content of the European species differed markedly from that of Canadian origin. Of the alkaloids found by Manske and Marion, Bertho and Stoll isolated annotinine and lycopodine, but failed to find obscurine, or alkaloids L.8, L.9, L.10, L.11, and L.12. They reported, however, the presence of acrifoline, previously isolated by Manske and Marion (7) from *L. annotinum* var. *acrifolium*, and several new bases—annotoxine, $C_{31}H_{42}O_5N_2$; annotine, $C_{16}H_{23}O_4N$; a base isomeric with lycopodine, $C_{16}H_{25}ON$; and another base, not well characterized, $C_{10}H_{19(21)}ON$. Achmatowicz and Rodewald found less difference between European and Canadian *L. annotinum* L. They established that annotine was incorrectly formulated and apparently identical to alkaloid L.11. Also it was shown that annotoxine was incorrectly formulated (it should be $C_{32}H_{44}O_5N_2$) and that it was a molecular compound of acrifoline, $C_{16}H_{23}O_2N$, and L.11, $C_{16}H_{21}O_3N$. In addition, they isolated annotinine, α- and β-obscurine (8), lycopodine, a base isomeric with lycopodine, L.8, and acrifoline. Of the alkaloids reported by Manske and Marion, only L.12, L.9, and L.10 are missing. Achmatowicz and Rodewald suggested that acrifoline might have been present in either of the two L.9 fractions reported by Manske and Marion (6), and that annotoxine was not isolated from the Canadian plant because the bases were separated by fractional crystallization of the perchlorates which would break down the molecular complex.

[1]*Manuscript received May 22, 1956.*
Contribution from the Department of Chemistry, Hamilton College, McMaster University, Hamilton, Ontario. Most of this work was taken from a thesis submitted by G. S. Perry to the Faculty of Graduate Studies in partial fulfillment of the requirements for the degree of Master of Science.

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Professor Bertho (3) recently stated that his group discovered in 1953 that annotoxine was a molecular compound of acrifoline and L.11, and that annotine was actually identical to L.11 (mixed melting point with a sample from Dr. Manske). He therefore assumed that the sample which they originally ascribed as a new alkaloid was simply a hydrate of L.11.

In their study of *L. annotinum* var. *acrifolium*, Manske and Marion (7) isolated annotinine, acrifoline, lycopodine, and four new alkaloids, L.28, L.29, L.30, and L.31, but failed to find obscurine, L.8, L.9, L.10, L.11, or L.12 which they found in *L. annotinum* L. However, later work by Douglas, Lewis, and Marion (5) has shown that L.8 and L.30 were identical. It would therefore seem that the differences between the two varieties are not so great as originally suspected by Manske and Marion (7). Compounds corresponding to L.28, L.29, and L.31 have not been reported by the European workers.

In the present work we were primarily interested in the chemistry of specific alkaloids and not in their relative abundance or occurrence in the plant. However, at various times we have isolated from *L. annotinum* of undetermined variety the following alkaloids: annotinine, lycopodine, obscurine, acrifoline, L.8, L.11, and L.12. From five different batches of plant material we have isolated annotoxine, which has been shown to be a molecular compound of acrifoline and L.11. The samples of plant material were derived from three different provinces, Nova Scotia, New Brunswick, and Ontario. Manske and Marion reported L.11 as characteristic of *L. annotinum* L. and acrifoline as characteristic of *L. annotinum* var. *acrifolium*. Our isolation of both alkaloids from a single preparation suggests that both alkaloids are probably present in at least one variety and perhaps in both, but were not detected by Manske and Marion possibly because of the isolation methods employed.

The chemistry of annotinine, lycopodine, and obscurine has been studied rather extensively, but the chemistry of the other alkaloids of *L. annotinum* has been dealt with only in a cursory fashion or not at all. Bertho and Stoll (4) reported that acrifoline contained no N—CH_3, O—CH_3, or OH groups, but apparently contained a carbonyl group on the basis of its ultraviolet spectrum and its reaction with phenyl lithium. Lack of reactivity toward peracetic acid and selenium dioxide led them to propose a fully saturated ring system for the alkaloid. Acrifoline did not undergo Hofmann degradation, but phenylacrifoline did. Likewise they stated that acrifoline did not hydrogenate, but gave no experimental details. They also stated that 2,4-dinitrophenylhydrazine gave no reaction, nor did treatment of the base with benzaldehyde and sodium ethylate.

Bertho and Stoll (4) reported that annotine (L.11) had no —OH, =N—CH_3, or —OCH_3 groups. However, it reacted with phenyl lithium and lithium aluminum hydride, but their interpretation of these reactions was complicated by their misconception concerning the correct molecular formula of the alkaloid. They reported with lack of experimental detail that annotine failed to react with benzaldehyde and sodium methylate, with hydrogen, with selenium dioxide, or with hydrazine. Neither did its methiodide undergo Hofmann degradation, nor would the alkaloid react with cyanogen bromide or hydrochloric acid.

No information on the nature of the function groups of L.8 or L.12 is recorded in the literature other than that L.8 is tertiary since it forms a methiodide on treatment with one mole of methyl iodide (1). Likewise acrifoline and annotine are tertiary bases (1).

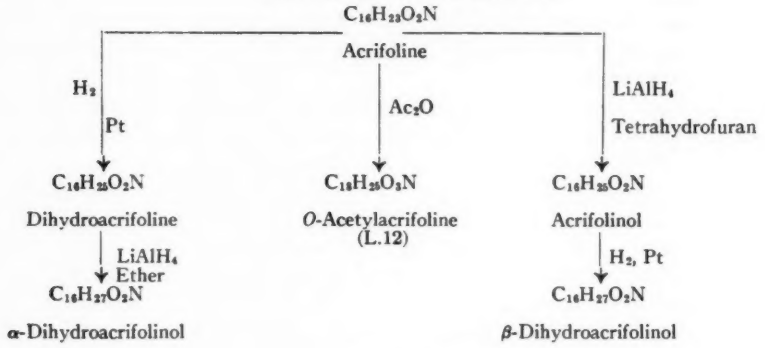
Our studies have established with reasonable certainty the nature of the functional groups in the four alkaloids, acrifoline, annotine (L.11), L.8, and L.12. Some other reactions of interest are also reported.

We have examined acrifoline by both infrared spectroscopy and chemical methods. The infrared spectrum of acrifoline in nujol showed very strong absorption in the hydroxyl region, but very weak absorption in the carbonyl region. However, in chloroform solution there was a strong band at 1700 cm.$^{-1}$ in the carbonyl region and another band at 1675 cm.$^{-1}$ which has been assigned to an unsaturated linkage. These functional groups have been confirmed by chemical treatment. Thus acrifoline underwent catalytic reduction over Adams' catalyst at 50 p.s.i.g. to give dihydroacrifoline which was analyzed as its hydrochloride and hydrobromide salts. Dihydroacrifoline was difficult to purify in a form suitable for analysis, but its infrared spectrum was examined and contained only hydroxyl and carbonyl absorption. We were unable to determine the degree of unsaturation of acrifoline in a microhydrogenation apparatus presumably because of insufficient pressure. This may explain the statement of Bertho and Stoll (4) that acrifoline failed to absorb hydrogen. Reduction of dihydroacrifoline by lithium aluminum hydride yielded α-dihydroacrifolinol, $C_{16}H_{27}O_2N$, which in its infrared spectrum contained hydroxyl but no carbonyl or double bond absorption. By hydride reduction of acrifoline in boiling tetrahydrofuran, the compound acrifolinol, $C_{16}H_{25}O_2N$, was obtained. This reduction failed to proceed in ether solution. Acrifolinol exhibited strong absorption in the infrared in the hydroxyl region, weak absorption in the unsaturation region, and no absorption in the carbonyl region. When acrifolinol was treated with hydrogen over Adams' catalyst, an isomeric β-dihydroacrifolinol, $C_{16}H_{27}O_2N$, was obtained which had an infrared spectrum similar, but not identical, to the α-compound. These two substances are undoubtedly stereoisomers; the isomerism could either be about the newly-formed hydroxyl group or about the centers of the original double bond in acrifoline.

Attempts to dehydrate acrifoline with boiling hydrochloric acid or phosphorus oxychloride led to recovery of starting material. However, treatment with acetic anhydride yielded a monoacetate, $C_{18}H_{25}O_3N$. This monoacetate melted at 119.2–120.2° C. and did not depress the melting point of a sample of alkaloid L.12, which was kindly supplied by Dr. R. H. F. Manske. The infrared spectra of the two compounds were also identical. Thus alkaloid L.12 is the *O*-acetyl derivative of acrifoline. The alkaline hydrolysis of alkaloid L.12 yielded acrifoline and thus no change in skeletal structure had occurred during the acetylation process.

The basicity constant, pK_a (pH at half titration), of acrifoline was found to be 8.34 while that of dihydroacrifoline was 9.13. The increase in basic strength on reduction can be accommodated on the basis of an allylamine structure for acrifoline. Increases of this order have been noted in similar cases (2). These results are summarized in the chart below.

REACTIONS OF ACRIFOLINE



The alkaloid annotine,[3] $C_{16}H_{21}O_3N$, has also been studied by infrared spectroscopy and chemical methods. The infrared spectrum contained a weak band in the hydroxyl region, a double peak in the carbonyl region, and weak absorption assigned to unsaturation. The presence of these functional groups has been confirmed by chemical methods.

Contrary to the report of Bertho and Stoll (4), we were unable to reduce this alkaloid by lithium aluminum hydride in either ether or tetrahydrofuran. However, it was reduced readily by sodium borohydride in ethanol to yield annotinol, $C_{16}H_{23}O_3N$. This base was crystallized from ethanol and isolated in a solvated form, but lost weight on drying corresponding to approximately two moles of ethanol. In its infrared spectrum the unsolvated base contained a double band in the hydroxyl region and weak absorption attributable to unsaturation, but no carbonyl absorption was present. Catalytic reduction of annotinol yielded dihydroannotinol, $C_{16}H_{25}O_3N$, which showed only hydroxyl absorption in the infrared region. As in the case of acrifoline, it was not possible to measure the unsaturation of annotine in a microhydrogenation apparatus. However, annotine did absorb one mole of hydrogen over Adams' catalyst at 50 p.s.i.g. to yield dihydroannotine, $C_{16}H_{23}O_3N$, which now showed hydroxyl and carbonyl absorption but no bands attributable to unsaturation.

The presence of a single carbonyl group in annotine was confirmed by its reaction with phenyl lithium to yield phenylannotine, $C_{22}H_{27}O_3N$. This compound showed no carbonyl absorption, and since only one mole of phenyl lithium had reacted, there must be present only a single carbonyl group in the alkaloid. The presence of a single hydroxyl function was demonstrated by conversion to a monoacetate which showed no hydroxyl absorption in the infrared. There was no structural change during the acetylation reaction since hydrolysis of the monoacetate regenerated annotine. The third oxygen of annotine must therefore be present as an ether.

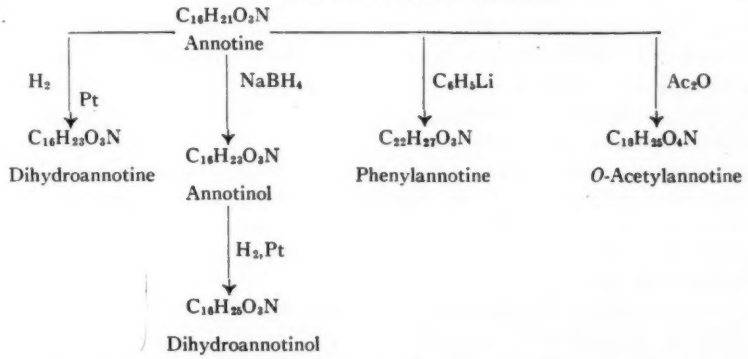
Unlike annotinine (7), the major alkaloid of *L. annotinum*, which also contains an ether function, the ether linkage in annotine is inert. Whereas an-

[3]*We have used the name annotine in the subsequent discussion in preference to the designation L.11 and we suggest that this name should be adopted for the alkaloid.*

notinine forms a chlorohydrin readily by the action of concentrated aqueous hydrochloric acid, annotine does not react in a similar fashion. Instead, treatment with boiling hydrochloric acid yielded an isomeric compound, $C_{16}H_{21}O_3N$, which contained no chlorine. The substance was isolated as its hydrochloride and although its infrared spectrum was very similar to annotine hydrochloride, the carbonyl band was shifted by 10 cm.$^{-1}$ and there were distinct differences in the 600–1200 cm.$^{-1}$ region. The present state of our knowledge does not allow an interpretation of this isomerization reaction. It would seem, however, that an epoxide group is not present in the alkaloid and that the ether ring must be of a larger size.

The basicity constants of annotine and dihydroannotine were found to be 7.5 and 8.61 respectively. This increase in basic strength on reduction is similar to the case of acrifoline and a similar interpretation can be drawn. The reactions of annotine are summarized in the chart below.

REACTIONS OF ANNOTINE



The other alkaloid which we examined was alkaloid L.8, $C_{16}H_{25}O_2N$. Our investigations were limited to an examination of its infrared spectrum which showed strong carbonyl and hydroxyl absorption; thus the alkaloid most likely contains one function of each type.

With a knowledge of the functional groups of these four alkaloids and their molecular formulas, it can be calculated that they all contain a basic tetracyclic ring system. In this respect they are similar to lycopodine and (if one excludes the ether and lactone rings) annotinine as well. Therefore it seems quite likely that all of these alkaloids may have a common tetracyclic ring system and be simple derivatives of one another.

EXPERIMENTAL

Annotoxine

The mother liquors remaining after the separation of annotinine from the mixed alkaloids of *L. annotinum* were set aside in the refrigerator and after several months a crystalline material separated. The crude alkaloid obtained by filtration melted at 190–191° C. After several recrystallizations from

acetone and methanol the compound melted at 196–197° C.[4] A mixed melting point with a sample of annotoxine provided by Professor Bertho showed no depression and their infrared spectra were identical. Calc. for $C_{32}H_{44}O_5N_2$: C, 71.61; H, 8.27; N, 5.22%. Found: C, 72.13, 72.12; H, 8.53, 8.28; N, 4.86, 4.80%. $[\alpha]_D^{19} = -187.1°$ ($c = 1\%$ chloroform). Values reported in the literature are $[\alpha]_D^{20} = -179°$ (chloroform) (3) and $[\alpha]_D^{19} = -185.6°$ (chloroform) (1).

The infrared spectrum[5] shows absorption in the hydroxyl region at 3400 cm.$^{-1}$, in the carbonyl region at 1730 cm.$^{-1}$ and 1695 cm.$^{-1}$, and a band at 1665 cm.$^{-1}$ probably representing unsaturation.

Separation of Annotoxine

(*a*) *By Chromatography.*—Annotoxine, 300 mgm., was dissolved in chloroform and adsorbed on an alumina column. The column was eluted with benzene and 10-ml. fractions were collected. Annotine passed through the column with benzene and from the combined fractions 130 mgm. of pure annotine was obtained. The column was then eluted with 2% methanol in benzene to yield first a sample of impure annotoxine (70 mgm.), m.p. 163–169° C., and then acrifoline (100 mgm.). Even after several attempts we were unable to obtain a sharp separation of the two alkaloids by this method.

(*b*) *Through the Hydrobromide Salts.*—A solution of 3 gm. of annotoxine in 100 ml. of hot acetone was made acid with 48% HBr whereupon there was immediate separation of a crystalline precipitate (1.66 gm.). Concentration of the mother liquors yielded an additional crop (0.3 gm.). The combined hydrobromides were dissolved in water, basified, and chloroform extracted. The dried chloroform extracts yielded, after evaporation of the chloroform, 1.40 gm. of acrifoline identified by its infrared spectrum and a mixed melting point with an authentic sample.

The acetone mother liquors remaining after the separation of acrifoline hydrobromide were taken to dryness. The residue was dissolved in water, basified, and chloroform extracted. The dried extracts yielded 1.5 gm. of annotine identified by its infrared spectrum and mixed melting point with an authentic sample.

Acrifoline

Acrifoline was available from annotoxine as above. It was also obtained by treatment of the crude alkaloid mixture (free of annotinine) with hydrobromic acid. Acrifoline was a pinkish-white solid which melted over a rather wide range, 99–104° C., even after several recrystallizations from ether. The mixed melting point with a sample provided by Dr. R. H. F. Manske showed no depression and the infrared spectra of the two were identical. Calc. for $C_{16}H_{23}O_2N$: C, 73.56; H, 8.81; N, 5.36%. Found: C, 73.20, 73.20; H, 9.06, 8.92; N, 5.0, 4.75%. $[\alpha]_D^{19} = -266.2°$ ($c = 1\%$ chloroform). Literature values are $[\alpha]_D^{20} = -250°$ (ethyl acetate) (3) and $[\alpha]_D^{21} = -264.8°$ (acetone) (1). $pK_a = 8.34$ (50% methanol–water).

[4]*All melting points are corrected.*

[5]*Infrared spectra were carried out in nujol mull unless otherwise specified and were determined on a Perkin-Elmer No. 21 recording spectrophotometer with a sodium chloride prism.*

The infrared absorption spectrum in nujol showed a strong band at 3310 cm.$^{-1}$ in the hydroxyl region and extremely weak absorption at 1700 cm.$^{-1}$ and 1670 cm.$^{-1}$. However, in chloroform solution there was very strong absorption at 1700 cm.$^{-1}$ and strong absorption at 1675 cm.$^{-1}$. These two bands are assigned to a carbonyl group and an unsaturated linkage respectively.

Attempts to determine the degree of unsaturation by microhydrogenation over a palladium catalyst in glacial acetic acid were unsuccessful. Under these conditions no hydrogen absorption occurred.

Annotine (L.11)

This alkaloid has so far been obtained only by the breakdown of annotoxine. After the alkaloid was recrystallized from methanol it melted at 174–176° C. A mixed melting point with a sample kindly provided by Dr. R. H. F. Manske showed no depression. Also the infrared spectra of the two samples were identical. $pK_a = 7.50$ (50% methanol–water), $[\alpha]_D^{19} = -114.5°$ ($c = 1\%$ $CHCl_3$). Literature values are $[\alpha]_D^{21} = -114°$ (chloroform) (3) and $[\alpha]_D^{24} = -110.3°$ (acetone) (1).

The infrared spectrum in nujol shows weak absorption at 3300 cm.$^{-1}$ in the hydroxyl region, and strong absorption at 1712 cm.$^{-1}$ and 1725 cm.$^{-1}$ in the carbonyl region; in carbon disulphide solution, strong absorption at 3550 cm.$^{-1}$ in the hydroxyl region; and in chloroform solution, strong absorption at 1720–1730 cm.$^{-1}$ in the carbonyl region, and at 1644 cm.$^{-1}$, which is tentatively assigned to unsaturation. Attempts to determine the degree of unsaturation by microhydrogenation were unsuccessful.

Alkaloid L.8

This alkaloid crystallized from an ether solution of some alkaloidal residues which had been freed of lycopodine and annotinine. It melted after several recrystallizations from ethanol at 179–181° C. The compound showed no depression in melting point on admixture with a sample kindly submitted by Dr. R. H. F. Manske. Also the infrared absorption spectra of the two were identical. Calc. for $C_{16}H_{25}O_2N$: C, 73.00; H, 9.51; N, 5.32%. Found: C, 72.60, 72.70; H, 9.36, 9.41; N, 5.40, 5.23%.

The infrared absorption spectrum shows a strong peak at 1710 cm.$^{-1}$ in the carbonyl region and at 3220 cm.$^{-1}$ in the hydroxyl region.

Attempts to prepare an acetyl derivative with pyridine – acetic anhydride have not been successful.

O-Acetylacrifoline (Alkaloid L.12)

A mixture of acrifoline (500 mgm.) and acetic anhydride (20 ml.) was refluxed for two hours. After it had been cooled, the anhydride was decomposed with ice water, the mixture basified with ammonia and extracted with chloroform. The dried extracts were concentrated and adsorbed on a column of alumina. Upon elution with chloroform a colorless band containing 250 mgm. of a white crystalline solid passed from the column. It was recrystallized from petroleum ether, m.p. 119–120° C. In admixture with an authentic sample of alkaloid L.12, $C_{18}H_{25}O_3N$, kindly given us by Dr. R. H. F. Manske, there was

no depression in melting point. Furthermore their infrared spectra were superimposable. There were no absorption bands in the infrared characteristic of hydroxyl, but instead two new bands at 1740 cm.$^{-1}$ and 1230 cm.$^{-1}$, attributable to an acetoxy group, were present in addition to the carbonyl band at 1715 cm.$^{-1}$.

We have also isolated a small sample of L.12 directly from the plant alkaloids. *O*-Acetylacrifoline readily undergoes alkaline hydrolysis to acrifoline.

Dihydroacrifoline

Acrifoline, 300 mgm., was dissolved in 50 ml. of redistilled methanol, treated with 0.10 gm. Adams' catalyst, and subjected to a hydrogen pressure of 50 p.s.i.g. for three hours. The yellow oil remaining after filtration and concentration was dissolved in ether and filtered to free it from a little insoluble material. The concentrated ether solution deposited almost colorless crystals after it had been standing several hours in the refrigerator. Several recrystallizations from ether gave a crystalline solid melting at 162.5–169.5° C. The free base, in pure form, was difficult to obtain in good yield. Consequently the combined mother liquors were evaporated to dryness, dissolved in acetone, divided, and converted into the hydrochloride and hydrobromide salts for analysis. Both salts had melting points greater than 300° C. Calc. for $C_{16}H_{25}O_2N.HCl$: C, 64.09; H, 8.74; N, 4.67%. Found: C, 63.51, 63.48; H, 8.70, 8.71; N, 4.80, 4.85%. Calc. for $C_{16}H_{25}O_2N.HBr$: C, 55.81; H, 7.61%. Found: C, 55.50, 55.43; H, 7.46, 7.42%. The infrared spectrum of the hydrochloride contained a strong band at 3240 cm.$^{-1}$ in the hydroxyl region, and at 1704 cm.$^{-1}$ in the carbonyl region. The spectrum of the hydrobromide contained bands at 3300 cm.$^{-1}$ and 1702 cm.$^{-1}$. $pK_a = 9.13$ (hydrochloride salt and water). The infrared spectrum of the free base contained strong absorptions at 3500 cm.$^{-1}$ in the hydroxyl region, and at 1679 cm.$^{-1}$ in the carbonyl region.

α-Dihydroacrifolinol

To a solution of 100 ml. of anhydrous ether containing 10 ml. of 2.76 *M* $LiAlH_4$ in ether there was slowly added a solution of 500 mgm. of dihydroacrifoline in 50 ml. of dry ether. The mixture was stirred under reflux for eight hours. Excess $LiAlH_4$ was destroyed by careful addition of aqueous ether, the ether layer was decanted, dried over anhydrous sodium sulphate, and concentrated. The yellow residue, 400 mgm. (80% theory), melted at 195.2° C. after recrystallization from methanol–acetone. Calc. for $C_{16}H_{27}O_2N$: C, 72.40; H, 10.26; N, 5.28%. Found: C, 71.80, 72.01; H, 10.12, 10.46; N, 4.79, 4.80%. Its infrared absorption spectrum contained a strong band at 3300 cm.$^{-1}$ in the hydroxyl region, but no bands attributable to a carbonyl group or an unsaturated linkage.

Acrifolinol

Acrifoline (1.50 gm.) was dissolved in 100 ml. of tetrahydrofuran dried over sodium. To this solution there was added 5 ml. of a 2.76 *M* solution of $LiAlH_4$ in ether, and the reaction mixture was refluxed with stirring for seven hours. Excess $LiAlH_4$ was destroyed by the careful addition of moist tetrahydrofuran and the reaction mixture filtered. On contact with air it became very dark

brown in color. After concentration, the dark brown residue was dissolved in 50 ml. dilute acetic acid, basified with ammonia, and extracted several times with chloroform. The combined chloroform extracts were dried and concentrated to yield 1.2 gm. of a light green foam which recrystallized from methanol. After several recrystallizations, it yielded colorless crystals, m.p. 191.1–192.6° C. Calc. for $C_{16}H_{25}O_2N$: C, 73.10; H, 9.57; N, 5.32%. Found: C, 72.40, 72.62; H, 9.57, 9.75; N, 4.84, 4.93%. The infrared spectrum showed strong absorption at 3266 cm.$^{-1}$ in the hydroxyl region, and weak absorption at 1425 cm.$^{-1}$ attributable to unsaturation.

β-Dihydroacrifolinol

A solution of 300 mgm. of acrifolinol in 50 ml. of redistilled methanol containing 0.10 gm. of Adams' catalyst was treated with hydrogen at a pressure of 50 p.s.i.g. for three hours. The solution was then filtered free of catalyst and concentrated to yield 300 mgm. of a crystalline solid which was recrystallized from acetone–methanol. The compound melted at 165.5–167.5° C. A mixed melting point with α-dihydroacrifolinol was depressed 40 degrees. Calc. for $C_{16}H_{27}O_2N$: C, 72.40; H, 10.26; N, 5.28%. Found: C, 72.17, 72.25; H, 10.03, 10.11; N, 4.70, 4.80%. The infrared spectrum contained a strong absorption band at 3290 cm.$^{-1}$ in the hydroxyl region. The spectrum was almost identical to that of α-dihydroacrifolinol.

Annotinol

A mixture of 0.10 gm. of sodium borohydride in 20 ml. of ethanol and 500 mgm. annotine in 15 ml. ethanol was refluxed for one hour, cooled, and excess borohydride destroyed by the addition of acetic acid. Most of the alcohol was distilled off, 50 ml. of water was added, and the solution was basified with ammonia. Chloroform extraction yielded 450 mgm. of a viscous oil which crystallized after standing 18 hr. Several crystallizations from ethanol yielded a crystalline compound which softened at 113–114.5° C. but was not completely molten until 129° C. It was dried at 78° C. and 0.01 mm. Hg pressure. The compound lost 27% of its weight on drying and then melted sharply at 131.5–132.5° C. The compound $C_{16}H_{23}O_3N.2C_2H_5OH$ would show a 25% loss in weight. Calc. for $C_{16}H_{23}O_3N$: C, 69.28; H, 8.36; N, 5.06%. Found: C, 69.34, 69.25; H, 8.17, 8.20; N, 5.45%.

In its infrared absorption spectrum the base contained a broad band in the hydroxyl region at 3550 cm.$^{-1}$, and weak bands at 1650 cm.$^{-1}$ and 1403 cm.$^{-1}$ attributable to unsaturation. In carbon disulphide solution there were two bands in the hydroxyl region at 3510 cm.$^{-1}$ (strong) and 3380 cm.$^{-1}$ (broad). There was also a band at 3022 cm.$^{-1}$ attributable to unsaturation.

Dihydroannotine

A solution of 100 mgm. annotine in 50 ml. of redistilled methanol containing 50 mgm. of Adams' catalyst was subjected to a hydrogen pressure of 50 p.s.i.g. for three hours. The solution was filtered free of catalyst and concentrated to yield 100 mgm. of product which crystallized immediately on contact with ether. Several recrystallizations from methanol yielded small white crystals of dihydroannotine, m.p. 201.5–202.5° C. Calc. for $C_{16}H_{23}O_3N$: C, 69.28; H, 8.36;

N, 5.06%. Found: C, 69.48, 69.33; H, 8.12, 8.20; N, 4.95%. $pK_a = 8.61$ (methanol). The infrared absorption spectrum contained a strong band at 3200 cm.$^{-1}$ in the hydroxyl region, and at 1728 cm.$^{-1}$ in the carbonyl region.

Dihydroannotinol

A solution of 300 mgm. of annotinol in 50 ml. of redistilled methanol containing 20 mgm. of Adams' catalyst was treated with hydrogen at 50 p.s.i.g. for three hours. The solution was filtered free of catalyst and evaporated to dryness to yield 300 mgm. of a brown viscous oil which crystallized immediately on contact with ether. After several recrystallizations from methanol, the compound melted at 185.8° C. Calc. for $C_{16}H_{25}O_3N$: C, 68.78; H, 9.02; N, 5.01%. Found: C, 68.35, 68.35; H, 9.07, 8.95; N, 4.82, 5.08%. The infrared absorption spectrum in carbon disulphide solution contained bands in the hydroxyl region at 3500 cm.$^{-1}$ (strong), and a broad band at 3290 cm.$^{-1}$.

O-Acetylannotine

A mixture of 15 ml. of acetic anhydride and 450 mgm. of annotine solution was heated under reflux for 30 min. The reaction mixture of this stage had become very dark. Excess acetic anhydride was decomposed by shaking with ice water, the solution basified with 20% sodium hydroxide solution and then extracted with chloroform until the extracts were colorless. The dried extract was concentrated and adsorbed on a column of alumina and eluted with chloroform. A colorless band rapidly passed through the column from which about 120 mgm. of a crystalline compound was obtained. After recrystallization from methanol it melted at 180.7–182.2° C. Calc. for $C_{18}H_{23}O_4N$: acetyl (1), 13.56%. Found: acetyl, 12.00, 12.65%. The infrared absorption spectrum showed strong bands at 1732 cm.$^{-1}$ and 1250 cm.$^{-1}$ attributable to the acetoxy group, and a band at 1715 cm.$^{-1}$ due to the carbonyl group.

Alkaline hydrolysis of the acetoxy compound above yielded annotine.

Phenylannotine

Phenyl lithium was prepared from 0.35 gm. lithium and 3.7 gm. of bromobenzene in 30 ml. of anhydrous ether. To the solution of phenyl lithium there was slowly added a solution of 900 mgm. of annotine in 100 ml. ether–benzene. During the addition a white complex separated out. The reaction mixture was refluxed for one hour following the addition of the annotine, then cooled and decomposed by pouring it onto ice containing glacial acetic acid. The organic layer was separated and the acid aqueous solution washed once with 50 ml. ether. The aqueous solution was then basified with 20% sodium hydroxide solution whereupon a white precipitate formed which was extracted with chloroform. The combined chloroform extracts were dried and concentrated to yield 1.30 gm. (93% theory) of a white crystalline product. The compound was refluxed with 250 ml. of acetone until dissolved, then concentrated to about 50 ml. and set aside to crystallize. The crystalline compound obtained softened at 130° C., but it was not completely molten until 213–214° C. It was crystallized again from acetone, but without change in the melting point. Upon drying under vacuum the compound lost 24% of its weight. The formula $C_{22}H_{27}O_3N.2CH_3COCH_3$ would accommodate a 24.7% loss in weight. The infrared spectrum of the undried compound contained very strong absorption

in the carbonyl region at 1710 cm.$^{-1}$. A sample was recrystallized from methanol to yield a product which melted, after drying under vacuum, at 214° C. In the infrared it contained no bands in the carbonyl region. The product first obtained from methanol was solvated since it lost 27.6% of its weight on drying corresponding to solvation by four moles of methanol. Calc. for $C_{22}H_{27}O_3N$: C, 74.75; H, 7.70%. Found: C, 74.30, 74.32; H, 7.70, 7.69%. In its infrared spectrum the dry material contained no bands in the carbonyl region. There was a strong band in the hydroxyl region at 3470 cm.$^{-1}$, and a weak band at 1640 cm.$^{-1}$ attributable to non-benzenoid unsaturation. There were strong bands in the 600–1200 cm.$^{-1}$ region attributable to a benzene ring.

Treatment of Annotine with Hydrochloric Acid

Annotine, 250 mgm., was refluxed for two hours with 20 ml. of 6 *M* hydrochloric acid. The acid solution was allowed to cool to room temperature, basified with ammonia, and then extracted several times with chloroform. The combined chloroform extracts were dried over sodium sulphate, and concentrated to yield 200 mgm. of a viscous brown residue which could not be induced to crystallize and gave a negative test for halogen (Beilstein test). Its infrared absorption spectrum contained bands at 3400 cm.$^{-1}$, 1735 cm.$^{-1}$, and 1662 cm.$^{-1}$, tentatively assigned to hydroxyl, carbonyl, and unsaturation respectively. The residue yielded a crystalline hydrochloride, which melted at a temperature greater than 300° C. Calc. for $C_{16}H_{21}O_3N.HCl$: C, 61.64; H, 7.07; N, 4.50%. Found: C, 61.62, 61.36; H, 6.91, 6.98; N, 4.24%. The infrared absorption spectrum of the hydrochloride contained a strong band at 3220 cm.$^{-1}$ in the hydroxyl region, a strong band at 1740 cm.$^{-1}$ with a shoulder at 1695 cm.$^{-1}$ in the carbonyl region, and weak absorption at 1420 cm.$^{-1}$ which is probably unsaturation.

A sample of annotine hydrochloride was prepared for comparison. It also melted above 300° C. Its infrared spectrum differed somewhat from that above. It contained a strong band at 3220 cm.$^{-1}$ in the hydroxyl region and strong carbonyl absorption at 1731 cm.$^{-1}$ with a shoulder at 1703 cm.$^{-1}$, but no band was detected in the 1400 cm.$^{-1}$ region. In the 600–1200 cm.$^{-1}$ region there were distinct differences between the two compounds.

ACKNOWLEDGMENTS

The authors wish to express their indebtedness to the National Research Council of Canada and to the Ontario Research Foundation for financial assistance. One of us (G.S.P.) acknowledges a grant from the Research Fund of the Chemical Society, London. We also wish to express our thanks to Professor K. Wiesner of the University of New Brunswick for a very generous donation of the crude alkaloids of *L. annotinum*.

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FURTHER OBSERVATIONS ON THE LEAD TETRAACETATE OXIDATION OF REDUCING DISACCHARIDES[1]

By A. J. Charlson[2] and A. S. Perlin

ABSTRACT

Evidence is presented which supports an earlier suggestion that the linkage-position in a reducing disaccharide may be determined readily by lead tetraacetate oxidation. Compounds examined include aldose and ketose disaccharides and aldobiuronic acids. Two types of reaction—one catalyzed by potassium acetate and the other non-catalyzed—are employed jointly to illustrate oxidation patterns which clearly differentiate each position of the biose linkage. Partial degradation of reducing disaccharides by lead tetraacetate oxidation is illustrated by the preparation of 2-*O*-α- and 2-*O*-β-D-glucopyranosyl-D-erythritol and 4-*O*-β-D-galactopyranosyl-D-erythritol. In turn, 2-*O*-β-D-glucopyranosyl-D-erythritol is degraded to 2-*O*-β-D-glucopyranosyl-glycerol.

A previous publication (16) described some oxidations of reducing disaccharides by lead tetraacetate. The reactions were carried out in aqueous acetic acid (2) using potassium acetate, which promoted catalysis of the carbohydrate oxidations and also permitted estimation of the formic acid released (15). Each position of the biose linkage was found to be associated with a distinctive oxidation pattern which readily differentiated it from other possible positions. It was therefore suggested that lead tetraacetate oxidation might be useful for determining the position of the linkage in a reducing disaccharide. The study has now been extended to include additional reducing disaccharides and some aldobiuronic acids which recently have become available to us. Other aspects of the lead tetraacetate oxidation of bioses are also considered in the light of recent findings with the normal (non-catalyzed) oxidation of monosaccharides (17).

The current results on structure determination are consistent with those obtained earlier (16), and the linkage-position determined for each compound is the same as that assigned by other investigators through the use of accepted methods. The data are summarized in Fig. 1 and Table I. As found previously, 1,6-aldohexopyranose disaccharides are degraded to a much greater extent than other linkage types, yielding about five moles of formic acid and consuming about six moles of oxidant. In contrast, 1,3- and 1,4-disaccharides yield little more than one mole of formic acid, most of which appears to be derived slowly from the non-reducing end-units. The latter two linkage types, however, are clearly distinguishable from each other in that the reducing end-unit of the former is cleaved only at the 1,2-hemiacetal glycol group to yield a pentose (monoformate), whereas that of the 1,4-compound is oxidized additionally at the 2,3-glycol group to give a tetrose (diformate).

These data are paralleled by results obtained from the structurally related 3-, 4-, and 6-mono-*O*-methyl-D-glucoses, allowance being made for the absence

[1]*Manuscript received June 1, 1956.*
Contribution from the National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan. Issued as Paper No. 227 on the Uses of Plant Products and as N.R.C. No. 4032.
[2]*National Research Council of Canada Postdoctorate Fellow, 1955–56.*

of a glycosidic non-reducing end-unit, which are virtually identical with the results reported previously for mono-*O*-methyl-D-galactoses. The behavior of 2-*O*-methyl sugars suggests that a disaccharide possessing a 1,2-linkage should be unique in readily yielding a mole of formaldehyde, since the primary alcohol group of the reducing end-unit would not be protected from oxidation either by the presence of a glycosidic linkage or by a formate ester group. This expectation has now been confirmed by lead tetraacetate oxidation of a known 1,2-disaccharide (7).

Two compounds, 4-*O*-β-D-mannopyranosyl-D-glucose and 4-*O*-β-D-mannopyranosyl-D-mannose, exhibit the only instances encountered of oxidation behavior which differs significantly from that expected. The reducing end-units of other 1,4-disaccharides examined—maltose, lactose, cellobiose, and 4-*O*-α-D-glucopyranosyl-D-mannose—are found to consume approximately two moles of oxidant within the first 15 min. reaction time (Table I and Ref. 16, Table I). This value, which is consistent with production of a tetrose from the reducing end-unit, is obtained by subtracting from the total consumption the quantity of lead tetraacetate consumed by the appropriate methyl monose glycoside. The latter quantity is assumed to approximate to the consumption of oxidant by the non-reducing end-unit. On the same basis, the reducing end-units of the mannosido-mannose and mannosido-glucose are found to consume only about one mole of oxidant, which corresponds to production of a pentose unit rather than the tetrose actually found. All other data (Fig. 1 and Table I), moreover, clearly indicate that the compounds should be assigned, correctly, a 1,4-linkage. In contrast, the reducing end-units of 3- and 6-*O*-α-D-mannopyranosyl-D-mannose are found to consume the predicted one mole and three moles of lead tetraacetate, respectively, by assuming that the α-mannopyranose non-reducing end-units are oxidized at the same rate as is methyl α-D-mannopyranoside. Since methyl α- and β-D-mannopyranosides are oxidized rapidly at about the same rate, the β-mannopyranose units of the two 1,4-disaccharides appear to possess an unusual ring conformation in solution, which is not easily attacked by lead tetraacetate.

The 1,4-ketohexose disaccharides, maltulose and lactulose, each liberate one mole of formic acid and consume three moles of lead tetraacetate. These results are consistent with those obtained with the aldose disaccharides and with the fact that ketose sugars yield esters of glycolic acid (17). Accordingly, the reducing end-units apparently consume only one mole of oxidant and are degraded to a glycolate ester of D-erythrose, and the non-reducing end-units yield formic acid at rates characteristic of other glucosides or galactosides. The 1,3-ketose disaccharide, turanose, shows behavior similar to that of the 2-substituted aldoses, being overoxidized by lead tetraacetate and yielding a mole of formaldehyde. These ketose disaccharides are thus comparable to aldose disaccharides in which the reducing end-unit is a pentose (compare 3-*O*-D-glucopyranosyl-D-arabinose with maltulose), differing in that the ester formed by cleavage of the hemiacetal glycol group is a glycolate, rather than a formate, ester.

Since the oxidation characteristics which distinguish a given linkage position

TABLE I

LEAD TETRAACETATE OXIDATION OF REDUCING DISACCHARIDES

Compound	$Pb(OAc)_4$ consumed[1]		Oxidation products		
	Total[2]	Reducing end[3]	Pentose[4]	Tetrose	Formaldehyde[4]
3-*O*-α-D-Mannopyranosyl-D-mannose	—	0.9	Arabinose (1.0)	0	—
3-*O*-α-D-Glucopyranosyl-D-glucose	—		Arabinose (0.8)	0	—
3-*O*-Methyl-D-glucose	1.1	1.0	—	—	—
4-*O*-β-D-Mannopyranosyl-D-mannose	4.3	1.2	0	Erythrose	0
4-*O*-β-D-Mannopyranosyl-D-glucose	4.1	1.1	0	Erythrose	0
4-*O*-β-D-Glucopyranosyl-D-mannose	4.1	2.2	0	Erythrose	0
4-*O*-β-D-Glucopyranosyl-D-glucose	4.0	2.1	0	Erythrose	0
4-*O*-D-Glucuronopyranosyl-D-galactose	4.9	—	0	Threose	Trace
4-*O*-(4-*O*-Methyl-D-glucuronopyranosyl)-D-galactose	2.7	—	0	Threose	Trace
4-*O*-Methyl-D-glucose	2.0	—	—	—	0
6-*O*-β-D-Glucopyranosyl-D-glucose	5.7	—	—	—	—
6-*O*-α-D-Mannopyranosyl-D-mannose	6.4	3.2	—	—	—
6-*O*-Methyl-D-glucose	4.3	3.0	—	—	—
2-*O*-Methyl-D-glucose	5.0	—	—	—	1.0
3 *O*-α-D-Glucopyranosyl-D-fructose	6.1	—	—	—	1.1
4-*O*-β-D-Galactopyranosyl-D-fructose	3.0	—	0	Erythrose	—
4-*O*-α-D-Glucopyranosyl-D-fructose	3.0	—	0	Erythrose	—
3-*O*-α-D-Glucopyranosyl-D-arabinose	3.2	—	0	Erythrose	—

[1]*Corrected by the amount consumed in oxidation of formic acid to* CO_2.
[2]*Five hours' reaction time.*
[3]*Fifteen minutes' reaction time; total consumption less the consumption by the corresponding methyl glycoside.*
[4]*Moles per mole.*

are associated chiefly with the reducing end of the disaccharide, the reactions described should also be of use with aldobiuronic acids, in which the non-reducing end-units are easily overoxidized by glycol-cleavage agents owing to the formation of an intermediate active methylene group (12). Thus, the oxidation of 6-*O*-β-D-glucuronopyranosyl-D-galactose at the outset resembles that of the 1,6-hexose disaccharides (Fig. 1), despite an eventual pronounced overoxidation. Paralleling the low acid yield from 1,4-hexose disaccharides, 4-*O*-D-glucuronopyranosyl-D-galactose gives much less acid than the 1,6-compound. Oxidation of the methoxyaldobiuronic acid, 4-*O*-(4-*O*-methyl-D-

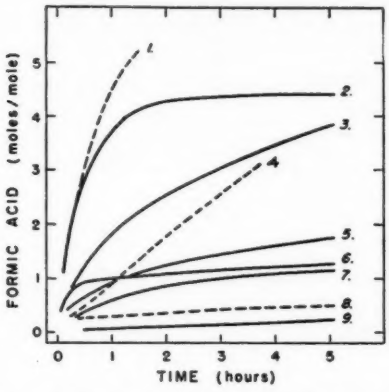

FIG. 1. Production of formic acid (evolution of carbon dioxide) during the lead tetraacetate oxidation of reducing disaccharides and aldobiuronic acids. (Compounds grouped together give identical or approximately the same rate curve; the data shown are for the first-named compound.)

1. 6-*O*-D-Glucuronopyranosyl-D-galactose
2. 6-*O*-α-D-Mannopyranosyl-D-mannose
   6-*O*-β-D-Glucopyranosyl-D-glucose
3. 3-*O*-α-D-Glucopyranosyl-D-fructose
4. 4-*O*-D-Glucuronopyranosyl-D-galactose
5. 3-*O*-D-Mannopyranosyl-D-mannose
6. 4-*O*-β-D-Galactopyranosyl-D-fructose
7. 4-*O*-D-Mannopyranosyl-D-glucose
   4-*O*-D-Mannopyranosyl-D-mannose
   4-*O*-β-D-Glucopyranosyl-D-mannose
   3-*O*-α-D-Glucopyranosyl-D-arabinose
   4-*O*-α-D-Glucopyranosyl-D-fructose
8. 4-*O*-(4-*O*-Methyl-D-glucuronopyranosyl)-D-galactose
9. 4-*O*-Methyl-D-glucose

glucuronopyranosyl)-D-galactose, illustrates more clearly the behavior of the reducing end-unit since the non-reducing end-unit of this compound does not yield formic acid and is not prone to overoxidation. Thus the formic acid production is only slightly greater than that from 4-*O*-methyl monoses, but the three moles of oxidant consumed correspond to formation of a tetrose diformate at the reducing end and cleavage of the 2,3-glycol group of the non-reducing end-unit. In agreement with these data, both 1,4-compounds yield threose (identified chromatographically) after oxidation and hydrolysis. A 1,3-linked aldobiuronic acid would be expected, accordingly, to yield one mole of pentose, and a 1,2-compound to give a mole of formaldehyde. The assignment of linkage position in aldobiuronic acids may be facilitated further by use of the oxidizing conditions considered below, in which complications due to overoxidation of the non-reducing end-unit are eliminated.

Studies on the reactions of monoses with lead tetraacetate have shown that aldoses and ketoses are degraded in a stepwise fashion, being attacked first at the hemiacetal glycol group (17). Since the rates of reaction of these compounds relative to those of glycosides (9, 15) are extremely rapid, it was to be expected that the reducing end-unit of a disaccharide should be degraded selectively under similar conditions, i.e., without potassium acetate and in the presence of only 1 to 2% of water. The rates of oxidation given in Fig. 2 are in agreement with this expectation. Aldose disaccharides possessing a 1,3-linkage quickly consume one mole of oxidant and further reaction is slow; the related 1,4-ketoses also consume one mole of oxidant rapidly. The aldose

unit of a 1,6-compound behaves similarly to an unsubstituted aldose, rapidly taking up two moles of lead tetraacetate. In contrast, aldohexopyranose disaccharides or aldobiuronic acids having 1,4-linkages are oxidized more slowly, possibly because they are unable to assume furanose ring forms (17), glucose units being less readily attacked than galactose units. The data obtained with the corresponding monomethyl aldohexoses are virtually identical, clearly indicating that the non-reducing end-units of the bioses are not attacked appreciably during the reaction period studied. This latter point is pertinent particularly for locating the linkage in aldobiuronic acids which, as noted above, may be overoxidized in the catalyzed reaction. Since the hemiacetal group of the 2-substituted sugars is blocked, these compounds are oxidized by lead tetraacetate at a relatively slow rate. The results therefore suggest that the non-catalyzed lead tetraacetate reaction may provide useful information, complementary to that obtained with the catalyzed reaction, for differentiating the various linkage types in disaccharides and aldobiuronic acids.

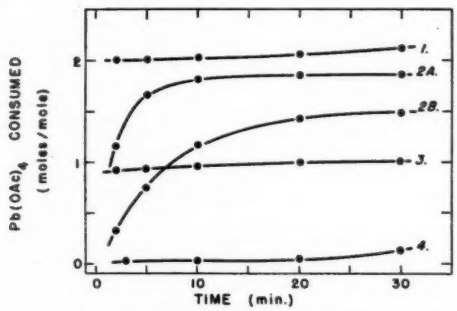

FIG. 2. Rates of lead tetraacetate consumption for reducing disaccharides, aldobiuronic acids, and mono-*O*-methyl hexoses. (Compounds grouped together give identical or approximately the same rate curve; the data shown are for the first-named compound.)

1. 6-*O*-D-Glucuronopyranosyl-D-galactose
6-*O*-D-Galactopyranosyl-D-glucose
6-*O*-Methyl-D-glucose

2A. 4-*O*-D-Glucuronopyranosyl-D-galactose
4-*O*-(4-*O*-Methyl-D-glucuronopyranosyl)-D-galactose
4-*O*-Methyl-D-galactose

2B. 4-*O*-α-D-Glucopyranosyl-D-glucose
4-*O*-Methyl-D-glucose

3. 3-*O*-α-D-Glucopyranosyl-D-arabinose
3-*O*-D-Mannopyranosyl-D-mannose
3-*O*-β-D-Glucopyranosyl-D-glucose
3-*O*-α-D-Glucopyranosyl-D-glucose
3-*O*-D-Galactopyranosyl-D-galactose
4-*O*-β-D-Galactopyranosyl-D-fructose
3-*O*-Methyl-D-glucose

4. 2-*O*-Methyl-D-glucose
2-*O*-Methyl-D-galactose

In addition to its value for the determination of structure, lead tetraacetate oxidation may be employed also for the preparation of some disaccharides by stepwise degradation of other disaccharides, in a manner already demonstrated with monosaccharides (17). To illustrate these possibilities melibiose, maltose, and cellobiose have been oxidized to give in high yields 4-*O*-α-D-galactopyranosyl-D-erythrose, and 2-*O*-α- and 2-*O*-β-D-glucopyranosyl-D-erythrose, respectively. The disaccharides were characterized as the crystalline glycosyl-erythritols. These reactions are equivalent to two successive single degradations by other procedures for descending the sugar series (6). Another possibility examined

was that of effecting a further controlled degradation starting from the glycosyl-erythritol. For the latter purpose, the fact that a polyol is more rapidly oxidized than a glycoside (8, 9) was utilized to degrade 2-*O*-β-D-glucopyranosyl-D-erythritol to 2-*O*-β-D-glucopyranosyl-L-glyceraldehyde which was reduced in turn, affording the known 2-*O*-β-D-glucopyranosyl-glycerol. This compound has been synthesized by Carter (4) from the intermediate formed by the Koenigs–Knorr reaction using tetraacetyl glucosyl bromide and 1,3-*O*-benzylidene-glycerol. The reaction sequence described therefore provides a possible synthetic pathway for glycosyl-erythritols and -glycerols, some of which are of natural occurrence (3, 13, 18) and, as noted elsewhere (5), may afford a definitive method for determining the configuration of the biose linkage in reducing disaccharides.

EXPERIMENTAL

The following compounds were obtained from the sources indicated in brackets: 3- and 6-*O*-α-D-mannopyranosyl-D-mannose (Prof. J. K. N. Jones); the barium salt of 4-*O*-(4-*O*-methyl-D-glucuronopyranosyl)-D-galactose (Dr. J. R. Nunn); nigerose (Dr. J. H. Pazur); 4-*O*-β-D-glucopyranosyl-D-mannose and 4-*O*-β-D-mannopyranosyl-D-glucose (Prof. F. Smith); the barium salt of 4-*O*-D-glucuronopyranosyl-D-galactose (Dr. A. M. Stephen); 4-*O*-β-D-mannopyranosyl-D-mannose (Prof. R. L. Whistler).

Other compounds were prepared by methods chosen from the literature or were obtained commercially.

The procedures used for determination of formic acid, lead tetraacetate consumption, pentose, and formaldehyde have been described previously (16).

Paper chromatography of the alcohols obtained from the degradation of disaccharides was carried out on Whatman No. 1 filter paper using butanol–ethanol–water (40: 11: 19 v/v) (11) as solvent and ammoniacal silver nitrate as spray reagent (14). The term R_{gal} denotes the rate of movement of the spots produced relative to galactose.

Solutions were concentrated at 40°C. *in vacuo*.

Examination of the Oxidation Products for Pentose or Tetrose Units

This was carried out as illustrated by the following example: 1.02 mgm. of 3-*O*-D-mannopyranosyl-D-mannose in 0.01 ml. of water was taken up in 0.1 ml. of acetic acid. Lead tetraacetate (4.0 mgm., 3 molar equivalents) in 0.4 ml. of acetic acid was added. Aliquots (0.05 ml.) of the solution were withdrawn at intervals for estimation of pentose; found: 1.06 moles (10 min.), 1.06 moles per mole (45 min.). Oxalic acid (10 mgm.) in acetic acid was added with stirring to the solution remaining, and 30 min. later the precipitate of lead oxalate was removed on the centrifuge. The acetic acid was evaporated off, the residue taken up in 0.2 ml. of water and heated in a sealed tube for three hours on the boiling water bath. The hydrolyzate, on examination by paper chromatography with various solvents, was found to contain only arabinose and mannose (aniline oxalate spray (10)) which, visually, were present in approximately equal amounts.

Measurement of Oxidation Rates in the Non-catalyzed Reaction

In a typical experiment 10 mgm. of maltose, dissolved in 0.2 ml. of water, was taken up in 10 ml. of acetic acid. Lead tetraacetate (200 mgm.), dissolved in 10 ml. of acetic acid, was added to the sugar solution. Aliquots (2 ml.) of the reaction mixture were removed at chosen intervals for the determination of lead tetraacetate consumed. The data are presented in Fig. 2.

4-O-α-D-Galactopyranosyl-D-erythritol

Lead tetraacetate (4.8 gm.) was added to a vigorously stirred solution of melibiose hydrate (1.8 gm.) in acetic acid (450 ml.) containing water (8.0 ml.). After six minutes' reaction time the solution gave a negative starch–iodide test. Oxalic acid dihydrate (0.5 gm.) in acetic acid (5 ml.) was then added, stirring being continued for an additional 30 min.; the lead oxalate was filtered off and the filtrate concentrated to dryness. The residue was taken up in water (30 ml.) and the solution was filtered, shaken with Amberlite IR–120 resin, and stored at 3°C. for 18 hr. The solution was deionized with a mixed-bed resin and concentrated, yielding a sirup (1.6 gm.). The latter, which did not crystallize and which streaked heavily on a paper chromatogram, was dissolved in water (30 ml.) and treated with sodium borohydride (400 mgm.) (1, 19). The resulting solution was kept at room temperature for 12 hr., then it was acidified with acetic acid, cations were removed with Amberlite IR–120 resin, the solution was concentrated to dryness, and boric acid was removed by repeated addition and distillation of methanol. After being taken up in methanol–ethanol the reduced product crystallized (0.9 gm.) and after one recrystallization from the same solvent had m.p. 133°C. and $[\alpha]_D^{25}$ +134° (*c*, 2, water). The compound (R_{gal}, 0.83) gave galactose and erythritol on acid hydrolysis (paper chromatographic identification). Calculated for $C_{10}H_{20}O_9$: C, 42.25%; H, 7.09%. Found: C, 42.11%; H, 6.99%.

On oxidation with lead tetraacetate – potassium acetate in acetic acid the compound yielded 1.9 moles of formic acid and consumed 5.8 moles of oxidant. Calculated for 4-*O*-α-D-galactopyranosyl-D-erythritol: formic acid, 2.0; lead tetraacetate consumption, 6.0 moles.

2-O-α-D-Glucopyranosyl-D-erythritol

Maltose (3.4 gm.), dissolved in water (8 ml.), was taken up in acetic acid (450 ml.) and treated with lead tetraacetate (9.2 gm.) for three hours. The addition of oxalic acid (2 gm.) in acetic acid (20 ml.) destroyed the excess lead tetraacetate and precipitated most of the divalent lead ions. The product was worked up and reduced with sodium borohydride (1 gm.) as described above. Yield, 2.8 gm. (R_{gal}, 0.90). Crystallization took place in methanol–ethanol, and after recrystallization from the same solvent the product had m.p. 147°–148°C. and $[\alpha]_D$ +130° (*c*, 1.8, water). Calculated for $C_{10}H_{20}O_9$: C, 42.25%; H, 7.09%. Found: C, 42.10%; H, 7.11%.

The compound (0.3 gm.) was acetylated by warming with acetic anhydride (2 ml.) and pyridine (0.8 ml.). The excess acetic anhydride was decomposed with ice water yielding a sirup which slowly crystallized. The acetate was

recrystallized from ethanol (yield 0.4 gm.), m.p. 97–98°C., $[\alpha]_D$ +105° (*c*, 1.2, chloroform). Calculated for $C_{24}H_{34}O_{16}$: C, 49.82%; H, 5.92%; acetyl, 52.1%. Found: C, 49.74%; H, 5.98%; acetyl, 52.2%.

2-O-β-D-Glucopyranosyl-D-erythritol

Cellobiose (3.4 gm.) was oxidized with lead tetraacetate (9.2 gm.) in acetic acid (600 ml.) containing water (10 ml.) for four hours. The product was worked up and reduced by the method described previously yielding a solid product (2.7 gm.) which was recrystallized from aqueous methanol (R_{gal}, 0.90); m.p. 185°–187°C., $[\alpha]_D$ −17° (*c*, 2.0, water). Calculated for $C_{10}H_{20}O_9$: C, 42.25%; H, 7.09%. Found: C, 42.38%; H, 7.10%. Oxidation with lead tetraacetate – potassium acetate in acetic acid—found: formic acid, 1.0 mole; lead tetraacetate consumption, 3.8 moles. Calculated for $C_{10}H_{20}O_9$: formic acid, 1.0 mole; lead tetraacetate consumption, 4.0 moles.

The heptaacetate of the disaccharide was prepared by the acetic anhydride – pyridine method. After recrystallization from ethanol it had m.p. 116°C. and $[\alpha]_D$ −1.4° (*c*, 1.6, chloroform). Calculated for $C_{24}H_{34}O_{16}$: C, 49.82%; H, 5.92%; acetyl, 52.1%. Found: C, 50.04%; H, 5.98%; acetyl, 51.8%.

2-O-β-D-Glucopyranosyl-glycerol

Lead tetraacetate (0.49 gm.) was added to a vigorously stirred solution of 2-*O*-β-D-glucopyranosyl-D-erythritol (0.31 gm.) in acetic acid (60 ml.) containing water (1 ml.). The solution was stirred for six hours and the product was isolated by the procedure described above. The sirup obtained (0.27 gm.) was dissolved in water (10 ml.) and reduced with sodium borohydride (0.1 gm.). The reduced product (0.26 gm.) was crystallized from methanol–ethanol. A paper chromatogram showed a major spot (R_{gal}, 1.33) and a faint spot (R_{gal}, 0.90). On acid hydrolysis, glucose and glycerol were produced (identified by paper chromatography). After recrystallization from methanol–ethanol the material had m.p. 163°C. and $[\alpha]_D$ −30.2° (*c*, 1.2, water). Calculated for $C_9H_{18}O_8$: C, 42.52%; H, 7.14%. Found: C, 42.78%; H, 7.13%. Carter reports m.p. 165°C. and $[\alpha]_D^{20}$ −30.1° for 2-*O*-β-D-glucopyranosyl-glycerol (4).

ACKNOWLEDGMENT

The authors express their gratitude to Prof. J. K. N. Jones, Dr. J. R. Nunn, Dr. J. H. Pazur, Prof. F. Smith, Dr. A. M. Stephen, and Prof. R. L. Whistler for the gift of samples. The assistance of Mrs. Carol Teed and of Mr. J. W. L. C. Christ in some of the experiments, and the microanalyses carried out by Mr. J. A. Baignée are acknowledged with thanks.

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THE PARTIAL MOLAL VOLUMES OF IONS IN AQUEOUS SOLUTION

I. DEPENDENCE ON CHARGE AND RADIUS[1]

By A. M. Couture and K. J. Laidler

ABSTRACT

The density data for aqueous solutions of electrolytes have been analyzed, and partial molal volumes at infinite dilution have been calculated. The values are shown to be additive, and a set of volumes for individual ions has been prepared, based arbitrarily on a value of zero for the hydrogen ion. It is shown that for a given value of the charge the volumes vary linearly with the cube of the ionic crystal radii, and for a given radius vary with the first power of the charge. In the case of cations the equation obeyed is

$$\bar{V}_+ = 16+4.9r^3-20z_+$$

while for anions

$$\bar{V}_- = 4+4.9r^3-20\,|z_-|.$$

If the volume of the hydrogen ion is taken as -6 ml. instead of zero the same equation is obeyed for both cations and anions, namely

$$\bar{V}'_\pm = 16+4.9r^3-26\,|z_\pm|.$$

The empirical equations are discussed in terms of a simple model for ions in solution.

INTRODUCTION

Although the partial molal volumes of ions are of some considerable theoretical and practical interest, particularly with reference to the effects of pressure on equilibria and rates, comparatively little work has been done on them. Owen and Brinkley (12) and Fajans and Johnson (3) have collected values for certain ions, and a few others have been quoted from time to time. The significance of the values has occasionally been discussed (3), but no attempt appears to have been made to analyze the volumes with a view to seeing how they depend on the valence (z) of the ion, the crystal radius (r), and other factors.

The present investigation has been concerned with obtaining a more complete and reliable set of values for ions of various types, and of showing empirically how the volumes of monatomic ions vary with z and r. Later publications will deal with the application of the results to pressure effects on equilibria and rates (8), and to obtaining empirical relationships in the case of polyatomic ions.

ANALYSIS OF EXPERIMENTAL DATA

There exist extensive data (6, 9) for densities (d) of aqueous solutions of electrolytes, and the apparent partial molal volume ϕ_v may be calculated from such densities using the formula (12)

$$[1] \qquad \phi_v = M/d_0-1000(d-d_0)/d_0c.$$

Here d_0 is the density of pure water at the temperature in question, c the concentration in moles per liter, and M is the molecular weight of the solute. For ionic solutes the Debye–Hückel theory predicts (5) that ϕ_v should vary

[1]*Manuscript received June 1, 1956.*
Contribution from the Department of Chemistry, The University of Ottawa, Ottawa, Canada.

linearly with the square root of the concentration, and many of the results have confirmed this relationship (2, 11, 12, 13, 15; see, however, Ref. 16). The procedure for calculating the partial molal volume at infinite dilution, $\bar{V}$, is therefore to plot ϕ_v values against $\sqrt{c}$ and to extrapolate to zero $\sqrt{c}$.

Proceeding in this way the table of values shown in Table I has been built up.

TABLE I

PARTIAL MOLAL VOLUMES OF IONIC SOLUTES (ML./MOLE)

Solute	$\bar{V}_{solute}$	Solute	$\bar{V}_{solute}$
HCl	18.1*	AgF	−3.1
LiCl	17.1*	$AgNO_3$	28.3*
LiBr	24.0*	$MgCl_2$	15.3*
LiI	35.6*	$CaCl_2$	18.5*
LiOH	−6.3*	$SrCl_2$	18.0*
NaCl	16.6*	$BaCl_2$	23.9*
NaBr	23.5*	$Cd(NO_3)_2$	38.0*
NaI	35.1*	$ZnSO_4$	−7.6
NaOH	−6.8*	$Pb(NO_3)_2$	42.5
Na_2SO_4	11.5*	$FeCl_2$	13.8
KF	6.6*	$FeBr_2$	23.0
KCl	26.8*	$FeSO_4$	−11.9
KBr	33.7*	$CoCl_2$	10.8
KI	45.3*	$CoBr_2$	23.8
KOH	3.4*	$Co(NO_3)_2$	30.6
KNO_3	38.0*	$CoSO_4$	−4.2
K_2SO_4	31.9*	$NiSO_4$	−10.1
RbCl	31.8*	$Al(NO_3)_3$	43.0
RbBr	38.7*	$AlCl_3$	12.9
RbI	50.3*	$LaCl_3$	16.0*
CsCl	39.2*	$Fe(NO_3)_3$	49.7
CsBr	46.1*	$Fe(NO_3)_3$	36.5†
CsI	57.7*	$CrCl_3$(violet)	13.9
TlF	10.5	$ThCl_4$	17.8
		$Th(NO_3)_4$	62.6

Quoted by Owen and Brinkley (12).
†*From Landolt-Börnstein (9); all other values from the International Critical Tables (6).*

This table includes most of the salts for which reliable data are available and which are known to be fully ionized and unhydrolyzed in dilute solutions. Compounds of B, Be, Hg (ic), and Hg (ous), and salts such as $FeCl_3$ and $ThCl_4$, are not included because there is evidence that they are not completely ionized in solution, while the following salts are omitted because there is evidence that they do not ionize to form simple ions: Au halides, Sn (ous) and Sn (ic) halides, and Cd halides; $AuCl_3$, for example, forms ions like $[Au(OH)_4]^-$ and $[AuCl_4]^-$. No reliable data appear to be available for salts of Tl^{+++}, In^{+++}, and Ga^{+++}.

Table II demonstrates the additivity of the partial molal volumes of ions, an effect that of course simply demonstrates the fact that the volumes are the sums of contributions for the individual ions. Various procedures for splitting the values for salts into ionic contributions have been suggested (1, 3), but since none is above criticism we have preferred to use the arbitrary procedure (also employed by Owen and Brinkley (12)) of taking the value for the proton as zero. Based on this convention our set of volumes, which confirm Owen and Brinkley's values where they are given, is shown in Table III. The values for

TABLE II

ADDITIVITY OF PARTIAL MOLAL VOLUMES OF IONS

	Cl		Br		I
Li	17.1	← 6.9 →	24.0	← 11.6 →	35.6
	↑		↑		↑
	−0.5		−0.5		−0.5
	↓		↓		↓
Na	16.6	← 6.9 →	23.5	← 11.6 →	35.1
	↑		↑		↑
	10.2		10.2		10.2
	↓		↓		↓
K	26.8	← 6.9 →	33.7	← 11.6 →	45.3

monatomic ions only are given in this table; those for other ions, together with a discussion of their significance, will be presented in a later publication. The values in Table III can readily be converted into values based on another standard; thus if the volume for the proton is actually X instead of zero, the values for cations will be raised by z_+X, where z_+ is the valence; the values for anions will similarly be lowered by $|z_-|X$, where $|z_-|$ is the absolute value of the valence of the ion (e.g. is +2 in the case of S^{--}).

Table III also includes the crystal radii of the ions, as given by Goldschmidt (4).

TABLE III

PARTIAL MOLAL VOLUMES OF IONS

($\bar{V}_{H^+} = 0$)

Ion	r(Å)	$\bar{V}_{ion}$ (ml./mole)	Remarks
Li^+	0.78	−1.0	From Owen and Brinkley (12)
Na^+	0.98	−1.5	From Owen and Brinkley (12)
K^+	1.33	8.7	From Owen and Brinkley (12)
Rb^+	1.49	13.7	From Owen and Brinkley (12)
Cs^+	1.65	21.1	From Owen and Brinkley (12)
Ag^+	1.13	−1.0	From Owen and Brinkley (12)
Tl^+	1.49	14.7	From TlF
H_3O^+	1.70	18.0	From Owen and Brinkley (12)
Mg^{++}	0.78	−20.9	From Owen and Brinkley (12)
Ca^{++}	1.06	−17.7	From Owen and Brinkley (12)
Sr^{++}	1.27	−18.2	From Owen and Brinkley (12)
Ba^{++}	1.43	−12.3	From Owen and Brinkley (12)
Cd^{++}	1.03	−20.6	From $Cd(NO_3)_2$
Pb^{++}	1.32	−16.1	From $Pb(NO_3)_2$
Zn^{++}	0.83	−22.1	From $ZnSO_4$
Fe^{++}	0.83	−25.3	Average from $FeCl_2$, $FeBr_2$, $FeSO_4$
Co^{++}	0.82	−24.6	Average from $CoCl_2$, $CoBr_2$, $Co(NO_3)_2$, $CaSO_4$
Ni^{++}	0.78	−24.6	From $NiSO_4$
Mn^{++}	0.80	−18.3	From $MnBr_2$
Al^{+++}	0.83	−43.1	Average from $AlCl_3$ and $Al(NO_3)_3$
La^{+++}	1.22	−38.3	From $LaCl_3$
Fe^{+++}	0.67	−44.6	From $Fe(NO_3)_3$—average of I.C.T. and L.B.
Cr^{+++}	0.65	−40.4	From $CrCl_3$(violet)
Th^{++++}	1.10	−54.6	From $ThCl_4$ and $Th(NO_3)_4$
OH^-	1.40	−5.3	From Owen and Brinkley (12)
F^-	1.33	−2.1	From Owen and Brinkley (12)
Cl^-	1.81	18.1	From Owen and Brinkley (12)
Br^-	1.96	25.0	From Owen and Brinkley (12)
I^-	2.20	36.6	From Owen and Brinkley (12)
S^{--}	1.84	−7.6	From Na_2S

DEPENDENCE ON CHARGE AND RADIUS

It is obvious from an inspection of Table III that the charge on the ion has an important effect on its partial molal volume. For a given radius each unit of charge lowers the volume by approximately 20 ml. In order to elucidate the effects of charge and radius the procedure was to determine the effect of radius for groups of constant charge, and then to study the charge effect separately. The monatomic cations present the most complete set of data, and it was found by trial that the volumes for these vary linearly with the cube of the crystal radii, the slope of the plot of $\bar{V}_+$ against r^3 being 4.9. The same relationship was found to apply to the other classes of ions.

In order to determine the dependence on z the values of $\bar{V}_+ - 4.9r^3$ were plotted against z. The result, shown in Fig. 1, demonstrates clearly that $\bar{V}_+$

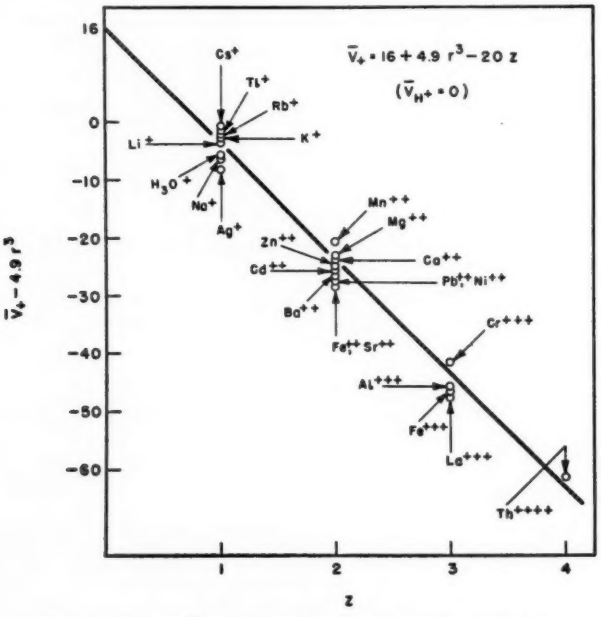

FIG. 1. Plot of $\bar{V}_+ - 4.9r^3$ against z for monatomic cations.

varies linearly with z. The intercept is 16 ml. and the slope -20, so that the empirical equation suggested by the results is

[2] $$\bar{V}_+ = 16 + 4.9r^3 - 20z_+.$$

A similar plot for the anions is shown in Fig. 2. Here the data are less extensive (there is only one point for $|z_-| = 2$) but the values are consistent with the same slope of -20, which leads to an intercept of 4. The empirical relationship obtained is thus

[3] $$\bar{V}_- = 4 + 4.9r^3 - 20\,|z_-|.$$

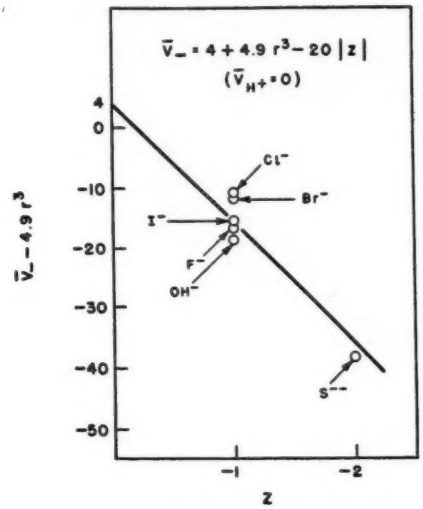

FIG. 2. Plot of $\bar{V}_- - 4.9r^3$ against z for monatomic anions.

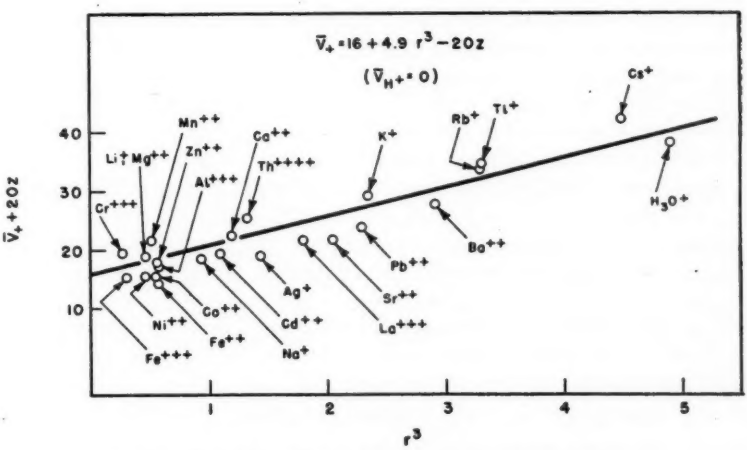

FIG. 3. Plot of $\bar{V}_+ + 20z_+$ against r^3 for monatomic cations.

The applicability of these relationships is further demonstrated in Figs. 3 and 4, which show plots of $\bar{V} + 20\,|z|$ against r^3. The linearity observed is quite satisfactory, the mean deviation of the volumes being 2.4 ml. in the case of the cations and 2.7 ml. in the case of the anions. Such deviations may be explained in part by errors in the volumes (as high as 5 ml. in the case of some of the polyvalent ions), and perhaps more importantly in terms of errors in the crystal radii. These latter errors are of course highly magnified by cubing

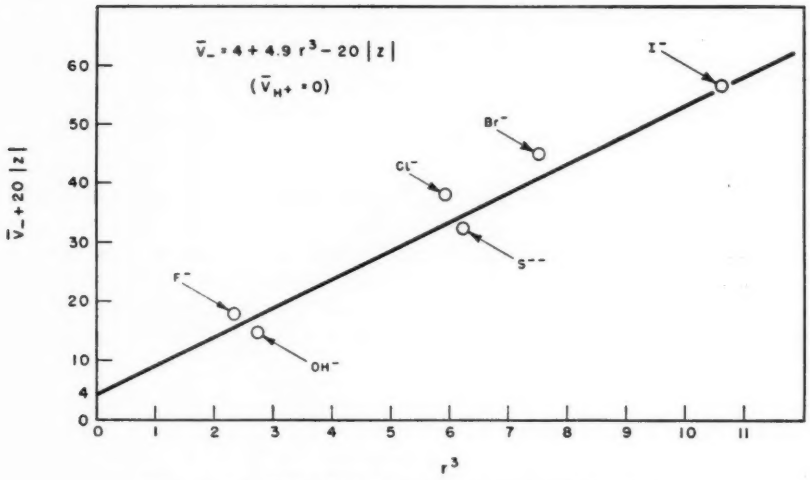

FIG. 4. Plot of $\bar{V}_- + 20\,|z_-|$ against r^3 for monatomic anions.

the radii. There are quite serious discrepancies between the crystal radii listed by Goldschmidt (4) and by Pauling (14), notably in the case of lithium for which the values are 0.78 Å and 0.60 Å respectively. In the present work the Goldschmidt values were found to give better correlations, and have therefore been used. In similar work on entropies (7) the univalent radii were found to give the best correlations, and there was little to choose between the Goldschmidt and Pauling values, presumably because $1/r$ was involved instead of r^3.

The empirical equations for cations and ions are seen to differ only in the constant term. This, however, is only a reflection of the arbitrariness in the choice of zero as the value for the proton. The two equations can be brought together if the values for all of the univalent cations are lowered by $\frac{1}{2}(16-4) = 6$ ml., and those for the univalent anions are raised by the same amount. This means that the new standard is $\bar{V}_{H^+} = -6$ ml., and accordingly the values must be lowered for all cations by $6z_+$ and raised for all anions by $6\,|z_-|$. If we define a new partial molal volume by $\bar{V}'_+ = \bar{V}_+ - 6z_+$, Equation [2] is transformed into

$$\bar{V}'_+ = 16 + 4.9r^3 - 26z_+. \qquad [4]$$

A similar procedure converts Eq. [3] into

$$\bar{V}'_- = 4 \mp 4.9r^3 - 14\,|z_-|. \qquad [5]$$

These equations are not in general identical, but become so for the particular case of $|z_-| = 1$. There is actually only one ion (S^{--}) for which $|z_-|$ is other than unity, so that with the exception of this case we may apply the general equation

$$\bar{V}'_\pm = 16 + 4.9r^3 - 26\,|z_\pm| \qquad [6]$$

to both cations and anions. Fig. 5 shows a plot of $\bar{V}'_\pm + 26\,|z_\pm|$ against r^3.

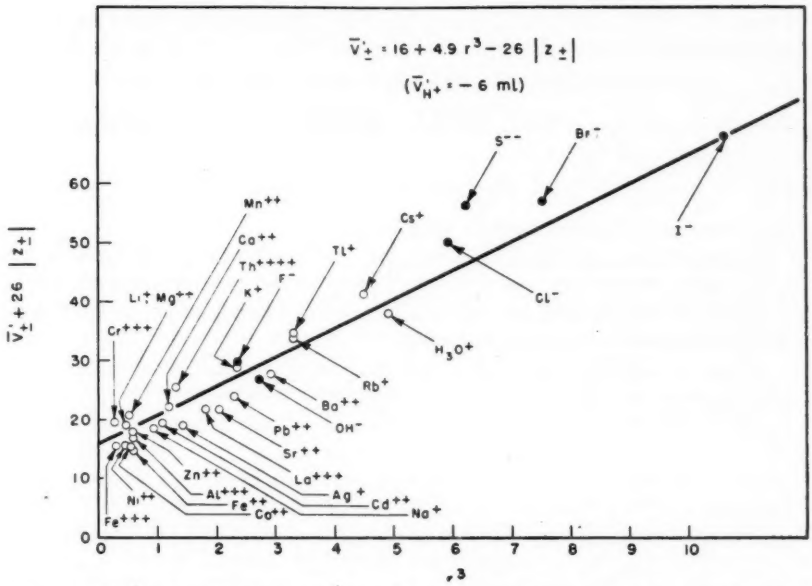

FIG. 5. Plot of $\bar{V}'_{\pm}+26\,|z_{\pm}|$ against r^3 for both monatomic cations and anions; $\bar{V}'_{\pm}$ is the partial molal volume relative to $\bar{V}_{H^+} = -6$ ml.

The correlation is satisfactory, and even the point for S^{--} is not too badly off the line. The mean deviation in this case is 2.7 ml.

DISCUSSION

The physical significance of the empirical equations that have been developed is not hard to understand. The volume occupied by an ion in aqueous solution may be considered to be made up of two terms: (1) a term related to the intrinsic volume of the ion itself, and (2) a term related to the electrostriction of water molecules in the neighborhood of the ion. On the simplest view the first of these terms would be simply $4/3.\pi r^3$, which works out to be $2.5r^3$ ml. per mole, where r is expressed in angstroms. The item that actually appears in the equations is $4.9r^3$, the numerical factor being approximately twice as great. The difference may be due to several causes. In the first place, the crystal radii are significantly smaller than the true radii of the ions owing to the distortion of the electronic orbitals in the crystal. Secondly, as indicated by the analysis of the entropies of ions (7), there is a free volume (of about 0.7 Å^3) associated with the ions in solution, and this must be added to the apparent volumes. These two factors seem to be quite sufficient to account for the apparent discrepancy between the coefficients of r^3.

In this connection it is of interest to note that Lee (10), on the basis of the partial molal volumes of uni-univalent electrolytes in aqueous solution, has proposed the equation

[7] $$V = 1.87(V_+ + V_-) - 20.7$$

where V_+ and V_- are the volumes of the ions in the crystals. Our Equations [2] and [3] lead to

$$[8] \qquad V = \bar{V}_+ + \bar{V}_- = 20 + 4.9(r^3_+ + r^3_-) - 20(z_+ + |z_-|) .$$

For the special case of a uni-univalent electrolyte this equation becomes, with $V_+ = 2.5r^3_+$ and $V_- = 2.5r^3_-$,

$$[9] \qquad V = 1.96(V_+ + V_-) - 20.$$

This equation closely resembles that of Lee.

The empirical equations obtained for ionic volumes are to be contrasted with those obtained (7) for ionic entropies, where a variation with z^2/r was found. It is of particular interest that entropies depend on z^2 (as predicted by the Born equation) and volumes on z.

It may be noted in conclusion that the present treatment makes no explicit reference to ionic hydration. The electrostriction terms in the empirical equations do in a sense cover the effects of hydration, but in our view the concept of ionic hydration has not proved to be a particularly useful one. The electrical field in the neighborhood of an ion falls continuously with increasing distance, and it is therefore arbitrary to regard some of the water molecules as associated with the ion and others as not. It is no doubt for this reason that different methods of measuring ionic hydration numbers lead to such widely different results.

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THE REACTIVE COMPONENTS IN ACTIVE NITROGEN AND THE ROLE OF SPIN CONSERVATION IN ACTIVE NITROGEN REACTIONS[1]

By H. G. V. Evans[2] and C. A. Winkler

ABSTRACT

Critical examination of the available experimental information provides rather convincing evidence that atomic nitrogen is the main reactive species in active nitrogen. It appears quite unlikely that a significant contribution to the activity is made by electronically excited molecules, metastable atoms, ions, or triatomic radicals. Evidence exists, however, for the presence of more than one active species, and a plausible suggestion would seem to be that the second species is vibrationally excited molecules. Consideration of the role of spin conservation in reactions of active nitrogen leads to the conclusion that reactions that conserve spin occur more readily than those in which spin is not conserved.

INTRODUCTION

A proposed unified interpretation (15) of the many reactions of active nitrogen that have now been studied made it essential to define as clearly as possible the nature of the reactive species in active nitrogen formed in a condensed electrical discharge. Numerous investigations into the properties of active nitrogen have been made and explanations of its behavior have been suggested from time to time. However, there is no recent critical evaluation which seeks to correlate all the results. Such an evaluation seems possible, and is attempted in the present paper, now that the dissociation energy of the nitrogen molecule has been established with virtual certainty.

THE REACTIVE COMPONENTS OF ACTIVE NITROGEN

Atoms and molecules in almost every conceivable excited state have been suggested as possible active species in active nitrogen. It is now widely accepted that the activity is due mainly, though perhaps not entirely, to atomic nitrogen (8, 12, 33, 45, 52, 56).

Electronically Excited Molecules and Atoms as Active Species

The $A^3\Sigma$ state should be the longest lived electronically excited state of molecular nitrogen.[3] During the emission of the Lewis–Rayleigh afterglow of active nitrogen the $A^3\Sigma$ state is continually being formed in small amounts because it is the lower state of the electronic transition $B^3\Pi \rightarrow A^3\Sigma$ that gives the afterglow (Fig. 1[4]). It has a lifetime with respect to radiation of 10^{-3} to 10^{-4} sec. (47) and must have a still shorter lifetime with respect to collisions to explain the absence of Vegard–Kaplan bands in the emission spectrum of

[1]*Manuscript received March 28, 1956.*
Contribution from the Physical Chemistry Laboratory, McGill University, Montreal, Quebec, with financial assistance from the National Research Council.
[2]*Holder of a National Research Council Studentship and Fellowship.*
[3]*The metastable $a^1\Pi_g$ state has also been suggested (43, 48) as a possible active species. This state is the upper state of the Lyman–Birge–Hopfield bands (Fig. 1) which appear to be more "allowed" than the "forbidden" Vegard–Kaplan bands emitted by the $A^3\Sigma$ state (27).*
[4]*Adapted from Ref. 51.*

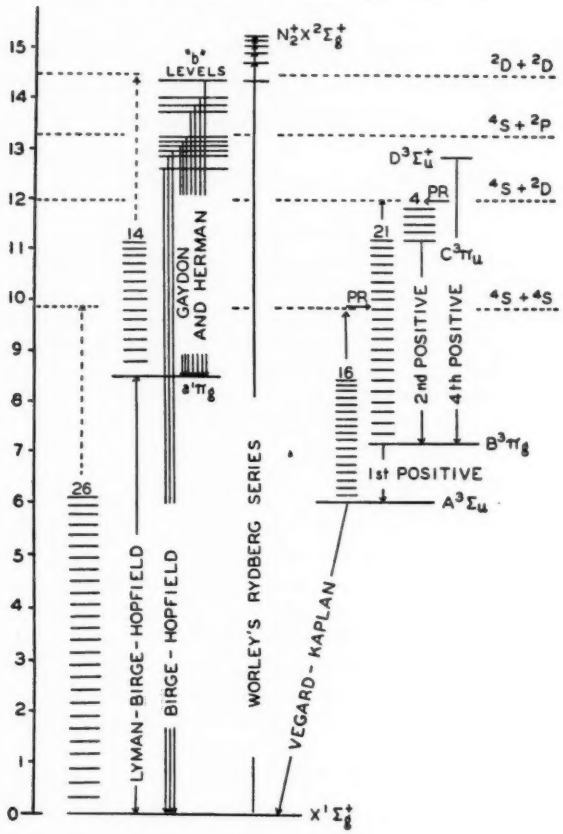

FIG. 1.

the afterglow. In the conventional fast flow systems used to study the chemical reactions of active nitrogen (e.g. 14), a lifetime of about 10^{-3} sec. for electronically excited nitrogen molecules formed in the discharge tube would mean that their concentration would be reduced by a factor of about 10^9 by the time they reached the reaction vessel. Since collisions will reduce the lifetime considerably below 10^{-3} sec., it seems quite certain that electronically excited nitrogen molecules formed in the discharge would not reach the reaction vessel in significant concentrations.

Benson (2) has suggested that emission of the afterglow occurs by metastable molecules going over into adjacent levels of the $B^3\Pi$ state (which emits the afterglow spectrum). He examined the transient response of the afterglow to the sudden increase in pressure caused by shock waves in active nitrogen and observed that the initial jump in intensity across the shock front depended on density instead of collision rate. By using interference filters, he found a marked difference in behavior of the yellow (5750±40 Å) and green (5640±

100 Å) parts of the spectrum. To reconcile these results with other work, if the dependence on density rather than collision rate is real, it would be necessary to assume that in the emission process an intermediate state is formed from nitrogen atoms by recombination in a triple collision and that this state has a lifetime of at least 10^{-4} sec. (The time of response of the photocells was less than 10^{-4} sec., and the radiative lifetime of B molecules is only about 10^{-8} sec.). However, the main evidence for the intensity dependence comes from measurements of intensities in the green spectral region, where the behavior is not what would be expected from either the known effects of increased pressure (39, 53) or the usual intensity distribution of the afterglow spectrum (51).[5] A little oxygen present in the shock tube experiments would result in emission of the green bands of nitric oxide (51) and it is perhaps well not to draw definite conclusions until this possibility has been examined experimentally.

Under special experimental conditions it is possible to excite other afterglows in nitrogen (34, 35, 36). These afterglows, in contrast to the Lewis–Rayleigh afterglow, have very short lifetime and show time-dependent intensity distributions in their spectra, which involve excited nitrogen molecules, molecule ions, and atoms.

The spectrum of the so-called "auroral" afterglow contains the forbidden Vegard–Kaplan bands emitted by nitrogen molecules in the metastable $A^3\Sigma$ state and forbidden lines emitted by nitrogen atoms in the metastable ^2P state (37, 38). The Lewis–Rayleigh afterglow, on the other hand, does not show either of these spectra, which indicates that neither of these metastable species is present in significant concentration in active nitrogen prepared by the usual methods (33).

This argument does not apply to atoms in the ^2D state in which the radiative lifetime is about 10,000 times that in the ^2P state (26). The magnetic resonance spectrum of active nitrogen (24) shows atomic nitrogen in the ^4S ground state to be present, but not the metastable ^2P and ^2D states. However, there should be nothing to prevent ^2D atoms from transferring their excitation energy in collisions of the second kind with other atoms. A careful search (23) showed no evidence for such resonance transfer in the spectra of metallic vapors excited by active nitrogen in a flow system, and it is probably safe to conclude that the concentration of excited nitrogen atoms is very low.

The fact that active nitrogen shows no absorption spectra in the region 2000 to 8700 Å (6, 25) is a further strong argument against the presence of significant concentrations of electronically excited nitrogen molecules and atoms in active nitrogen. All the known excited states would show absorption in this region (Fig. 1, Ref. 51). On the other hand, the first allowed transitions for nitrogen atoms and molecules in the ground state lie in the far ultraviolet.

[5] *Benson's explanation of the selective enhancement of one part of the spectrum does not appear to be acceptable. The most intense bands in both spectral regions selected by the filters used arise from transitions from the same vibrational levels of the B state going to different levels of the A state and the relative intensities are the same (56) so that a change in population in the vibrational levels of the B state would not give an increased intensity in only one region. Benson shows a photograph of the spectrum of the afterglow in active nitrogen flowing through a nozzle at supersonic velocity. There is no indication of any change in the relative intensities of different parts of the spectrum in going from the high pressure to the low pressure side.*

Nitrogen atoms in the metastable ^2P and ^2D states, and molecules in the metastable $A^3\Sigma$ state, have been introduced into mechanisms for afterglow emission for two main reasons: (i) to explain the selective enhancement of certain vibrational levels in the emission of the afterglow (8, 9, 49), and (ii) to explain the excitation of 9.6 ev. emission with only 7 ev. presumed available from recombination of two atoms in the ^4S ground state (8, 9). The adoption of 9.76 ev. for $D(N_2)$[6] prevents the operation of the first of these processes (56) and removes the necessity for explaining the second. Moreover, these mechanisms cannot explain the termolecular kinetics of the decay process (39, 53, 70, 72, 73) and the observed constancy in the relative intensities of different parts of the afterglow spectrum during the decay (9).

Charged Particles as Active Species

At one time Mitra (44) suggested that the activity of active nitrogen was due to the presence of N_2^+ ions. This theory was based on analogous processes that were thought to occur in the emission of the spectrum of the night sky, and on the very large energies transferred to metal foils in some experiments made by Lord Rayleigh (54). It has since been found that the interpretation of the atmospheric spectrum in terms of N_2^+ was wrong (7) and that Rayleigh's results were due to bombardment by electrons from the exciting discharge (2). Mitra has therefore suggested recently (45) that the activity of active nitrogen is due to nitrogen atoms.

In the absence of an ion trap after the exciting discharge, streaming active nitrogen contains a very low concentration of electrons (less than one free electron for 10^6 molecules of nitrogen (2, 10)). Such a low concentration of free electrons should not affect processes occurring in the gas phase to any extent, but might affect processes on the walls of the system.

The physical properties of active nitrogen are not changed by the removal of charged particles (2, 63)[7] and it seems unlikely that charged particles have an appreciable effect on the chemical reactivity of active nitrogen.

Atoms in the ^4S Ground State as Active Species

The long life of active nitrogen (52) and its sensitivity to wall conditions (22, 55) are immediately explained if atoms are the active species, and their presence has been shown directly by the excitation of the atomic lines with an auxiliary discharge (1), by Wrede gauge measurements (75), by the magnetic resonance spectrum (24), and by the mass spectra (29). The most convincing evidence that they play the principal role in the emission of the active nitrogen Lewis–Rayleigh afterglow comes from the termolecular kinetics of the decay process (39, 53, 70, 72).

The ability of active nitrogen to take part in resonance transfers of large

[6]*It now appears that the experimental (13, 16, 22, 37, 65) and theoretical (18, 20, 40) evidence is overwhelmingly in favor of 9.76 ev. for $D(N_2)$.*

[7]*Kane and Clark (31) found that a magnetic field reduced the rate of decay of the afterglow by about 3% and concluded that ions must take a part in the emission process. In view of all the other evidence, it seems likely that their interpretation of the results was incorrect, and that the effect was due to some other cause, such as change in surface condition.*

amounts of energy in exciting atomic and molecular spectra (30, 38, 51) was largely responsible for the original suggestion (4, 46, 57) that electronically excited molecules must be present. This is not really necessary, however, since there seems to be no reason why the inverse of a photosensitized dissociation should not occur,

$$N + N + X \rightarrow N_2 + X^*.$$[8]

The potential energy surfaces are the same for the reaction in either direction, and it is probable that the critical configuration would be very similar to that for the process

$$N_2^* + X \rightarrow N_2 + X^*.$$

The recombination of hydrogen atoms can excite the sodium *D* lines, and the 2537 Å line of mercury (5), and presumably nitrogen atoms might behave the same way.

The emission of electrons from metal surfaces exposed to active nitrogen (11) is somewhat more difficult to understand, but the candoluminescence observed when various activated oxides are exposed to hydrogen atoms (58) shows that atom recombination can transfer large quanta of energy to solid surfaces.

The fact that an auxiliary mild electric discharge through active nitrogen extinguishes the afterglow and excites the fourth positive bands of molecular nitrogen (63) has been interpreted (9, 32) to mean that significant concentrations of excited nitrogen molecules in metastable states are present in active nitrogen. However, in normal nitrogen a condensed discharge is required, both to excite these bands and to form nitrogen atoms (60). Hence, these results might only indicate the similarity of the conditions prevailing in a mild discharge through active nitrogen to those in a condensed discharge through normal nitrogen, where both atoms and electrons are certainly present. Wrede found (75) direct evidence that a discharge removed atoms very readily.

It has been observed that the visible afterglow disappears in a heated section of a flow tube and reappears downstream (63), and that if the glass is heated strongly enough to give off some sodium, the "dark modification" of active nitrogen can still excite the sodium *D* lines (9, 32). This has been interpreted as evidence for the presence of two active species (9, 32, 70, 72). However, these results can be interpreted just as readily if atomic nitrogen is the only active species, since the recombination process leading to the afterglow is known to have a negative temperature coefficient (53). If the extinction of the afterglow occurs because an active species is being destroyed in the hot zone, it is difficult to understand how the afterglow can reappear downstream.

Vibrationally Excited Molecules in the Ground State as Active Species

The assumption that nitrogen atoms in the ^4S ground state are the most important active species in active nitrogen makes it possible to suggest energetically reasonable mechanisms for its chemical reactions. However, recent work in this laboratory has given evidence, discussed later, that a second species of lower reactivity than atomic nitrogen is present in active nitrogen in

[8] *The symbol * represents electronic excitation.*

significant concentrations.[9] To explain the results it is only necessary to assume that the second species can transfer quite large amounts of energy in collisions of the second kind. The previous discussion would seem to rule out all the species hitherto suggested. The only species that might behave in this way, and should be present in significant concentrations, appears to be *vibrationally* excited nitrogen molecules.[10] None of the objections raised against electronically excited metastable states would apply to vibrationally excited molecules in the ground state.[11] It is well known that homonuclear diatomic molecules are very stable with respect to radiation of vibrational quanta (28) and that they may retain their vibrational energy over many thousands of collisions (42, 50). Molecular systems are very reluctant to transfer quanta of energy that are large compared with kT from internal degrees of freedom into translational motion. This means that when electronically excited nitrogen molecules are deactivated by collision they will go over into the adjacent upper levels of the ground state. Thus, the formation of short-lived electronically excited states by recombination of nitrogen atoms and in the parent discharge must ultimately lead to the formation of nitrogen molecules in the highest vibrational levels of the ground state.

Some idea of how fast such molecules will lose their energy may be obtained from the experimental results for the first excited vibrational state of CN. The probability of transfer of vibrational energy is mainly determined by the energy gap between successive vibrational levels. The gap between the first two levels of CN is 2024 cm.$^{-1}$, which is between 2331 and 1556 cm.$^{-1}$, the values for the first two levels and the last two observed levels of N_2 (28, Table 39). The collision yield for deactivation of the first excited vibrational level of CN is about 10^{-4} in pure cyanogen and about 10^{-5} in argon (68). For typical experimental conditions that have been used to study the reactions of active nitrogen, excited nitrogen molecules will undergo about 10^7 collisions per second, so that the rate constant for collisional deactivation should be between $k = 10^2$ sec.$^{-1}$ and $k = 10^3$ sec.$^{-1}$.[12] If it is assumed, for simplicity, that the rate of deactiva-

[9]*The possible presence of an unidentified second active species in active nitrogen has been suggested earlier (70, 71, 74). However, the amount of active species was estimated from the amount of nitric oxide decomposed in the nitric oxide – active nitrogen reaction, and the mechanism of this reaction is probably complex (59). Hence, the significance of the results is somewhat doubtful.*

[10]*Triatomic radicals (N_3) have been proposed as a possible reactive species (64, 66). The possibility that significant concentrations of these radicals (with long enough lifetime to be distinguished from N–N_2 complexes) are present in active nitrogen appears to be ruled out by the termolecular kinetics of the afterglow decay, and its long lifetime. If N_3 radicals were present, and able to react with other molecules, it seems reasonable that they would react fast with nitrogen atoms.*

[11]*The transparency of active nitrogen from 2000 Å to 8700 Å does not rule out the presence of vibrationally excited molecules in the upper vibrational levels of the ground state, even though part of the Lyman–Birge–Hopfield bands (with those levels as the lower state) do lie in this region. The Lyman–Birge–Hopfield bands result from a forbidden transition and are about 2000 times weaker than the allowed transitions of electronically excited atoms and molecules (27). Since the part of the system that extends beyond 2000 Å is still weaker than the main part of the system, only a very high concentration of vibrationally excited molecules could be detected by absorption in the region 2000 Å to 8700 Å.*

[12]*A recent study (42) has shown that in the collisional deactivation of vibrationally excited oxygen molecules, the energy is removed most readily when there is near resonance of the vibration levels of the collision partners. For deactivation of O_2 by N_2 or argon, the collision yield is less than 10^{-7}, which indicates that these estimates for k may be somewhat high.*

tion is the same for all vibrational levels, it is possible to derive an expression (Appendix) for the fraction of molecules which have lost j quanta

$$M_{n-j}/M_n{}^0 = x^j e^{-x}/j!$$

where $M_n{}^0$ = initial concentration in the nth vibrational level,
M_{n-j} = concentration in the $(n-j)$th level,
x = kt, where k is the mean rate constant and t is the time.

Fig. 2 shows the distribution curves for three values of kt. It has been assumed that all the excited molecules were initially in the highest observed level. In the apparatus used to study reactions of active nitrogen, the time required for the gas stream to pass from the discharge tube to the reaction vessel is

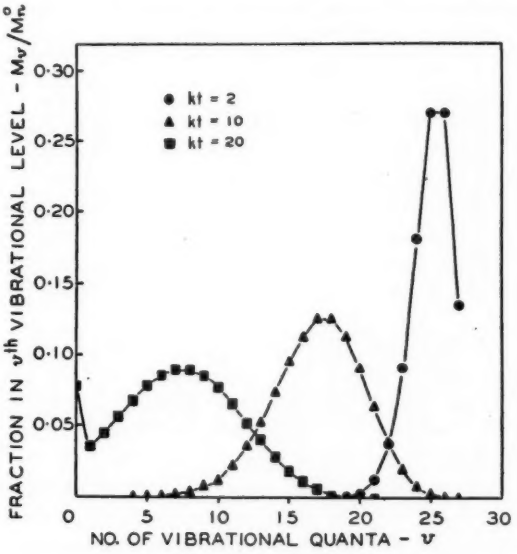

FIG. 2.

generally about 0.02 sec. Hence, the distribution curves of Fig. 2 will give the distribution of excited molecules reaching the reaction vessel for two extreme values and an average value of k. The most highly populated levels have excitation energies of about 140, 98, and 42 kcal. for kt values of 2, 10, and 20 respectively. It seems likely that these energies are, if anything, rather too low, since there must be several widely spaced levels above the highest observed level.[13]

Recently, a mass spectrometric analysis of active nitrogen has been made (29). The appearance potentials of the mass 14 and 28 peaks were compared with those from normal nitrogen. The ion current vs. electron energy

[13] *Extrapolation of the observed levels from the highest observed level (at 6.6 ev. above the zero level) to the dissociation limit at 9.76 ev. shows that the potential curve does not decrease markedly in slope until well above the last observed level (19).*

curves from the mass 28 peaks were superimposable, but those for the mass 14 were quite different. The mass 14 curve of active nitrogen showed an inflection that indicated N^+ ions to be formed by two processes with appearance potentials of 14.7 and 16.1 ev. The first value corresponds closely to that expected for the process

$$N(^4S) + e \rightarrow N^+ + 2e$$

which provides direct evidence for the presence of ^4S atoms in active nitrogen. If the second process is

$$N_2\dagger + e \rightarrow N(S^4) + N^+ + 2e$$ [14]

with an appearance potential of 16.1 ev., $N_2\dagger$ molecules with excitation energies greater than 8 ev. must be present in active nitrogen.

While there would seem to be a good possibility for a significant concentration of molecules with more than 100 kcal. of vibrational excitation to be present in the reaction vessel, the average time spent in the reaction vessel is generally about 0.2 sec., and most of the excited molecules should have time to pass their excitation energy to other molecules. Since the principle of resonance is approximately obeyed for the transfer of vibrational energy, and the vibrational quanta of the nitrogen molecule are between 4.5 and 6.6 kcal., foreign molecules should have a good chance of acquiring 5 kcal. or more of vibrational energy. This means that the vibrational temperature in the reaction vessel might be much higher than the translational temperature, particularly since nitrogen atoms must give products with considerable vibrational energy. Thus, considerable caution must be exercised in interpreting measured activation energies.

In view of the arguments advanced above in favor of only one-quantum transfers, it may well be asked how vibrationally excited nitrogen molecules may be an active species that can transfer all, or nearly all, their excitation energy in collisions of the second kind. The answer might lie in the presence of neighboring electronically excited states (Fig. 1). Transfer from the potential curve of the ground state to the potential curve of, for example, the $A\,^3\Sigma$ state might well occur during a collision provided the internal energy were sufficient. Such a process would be the inverse of the collisional deactivation of the $A\,^3\Sigma$ state which, as indicated previously, is known to occur quite readily. Since both the nitrogen and its collision partner must be considered, the process must be described in terms of multidimensional potential energy surfaces, the resonance transfer of energy occurring by a radiationless transition from one surface to another corresponding to a different electronic configuration. This picture is essentially similar to that which has been suggested (41) to explain the chemiluminescent emission of the sodium D lines (3) produced by vibrationally excited sodium chloride molecules:

$$NaCl\dagger + Na \rightarrow Na^* + NaCl^*.$$

The presence of electronically excited states adjacent to the upper vibrational levels of the ground state of N_2 implies that the change in electronic configuration can occur without marked interaction between N_2 and the

[14] *The symbol † represents vibrational excitation.*

collision partner. Thus, the resonance transfer process might be described somewhat schematically as follows:

(i) formation of a collision complex (on the ground state potential surface)

$$N_2\dagger + X \rightarrow N_2\dagger - - - X$$

with a sufficient lifetime to permit

(ii) attainment of the configuration required to cross to the potential surface corresponding to electronic excitation

$$N_2\dagger - - - X \rightarrow N_2^* - - - X \text{ (critical configuration)}$$

and (iii) separation of products on the excited potential surface with the collision partner receiving the electronic excitation energy

$$N_2^* - - - X \rightarrow N_2 + X^*.$$

The third step may be regarded as a resonance transfer of electronic excitation energy. Such transfers are known to occur readily when there is a close match of excitation energies. Since $N_2\dagger$ molecules in active nitrogen may have excitation energies considerably above the dissociation limits of most other molecules, perfect resonance should be possible between this excitation energy and the excitation energy of the continuous excited state of the collision partner. Thus, resonance transfer from $N_2\dagger$ to most other molecules should lead to dissociation of the collision partner.

If $N_2\dagger$ molecules can behave as discussed above, the rather puzzling results obtained from a study of the reaction of active nitrogen with mixtures of ammonia and ethylene (17) can be explained. At sufficiently high ammonia flow rates the limiting amount of ammonia decomposed did not change when ethylene was added, but the amount of HCN formed from ethylene was decreased in the presence of ammonia.[15] These results can be explained by the reaction scheme:

$$NH_3 + N_2\dagger \rightarrow N_2 + NH_3^* \rightarrow N_2 + NH_2 + H, \quad [1]$$

$$NH_2 + N \rightarrow N_2 + 2H, \quad [2]$$

$$N + C_2H_4 \rightarrow HCN + CH_3, \quad [3]$$

$$N + CH_3 \rightarrow HCN + 2H. \quad [4]$$

It is necessary to assume further that:

(i) the reaction of nitrogen atoms with radicals (reactions [2] and [4]) is very fast compared with the reaction with ethylene (reaction [3]);

(ii) reaction [1] is fast enough to give complete consumption of $N_2\dagger$ molecules when ammonia is present in sufficient excess, and the concentration of $N_2\dagger$ molecules is only about 15–20% of the concentration of atomic nitrogen;

(iii) the direct reaction between ammonia and nitrogen atoms is slow compared with reaction [3].

The first assumption receives support from theory and from experimental

[15] *Recent work by Armstrong and Winkler has shown that an increase in voltage across the nitrogen discharge, with other operating conditions constant, caused a marked increase in the ratio of the maximum amount of ammonia decomposed to the maximum yield of hydrogen cyanide from ethylene. This behavior gives strong support to the assumption of two reactive species in active nitrogen.*

observations in other reactions (see below). The third is not unreasonable in view of the behavior of other simple hydrides, e.g. H_2, H_2O, CH_4, all of which are relatively inert to nitrogen atoms. The main reasons for the inertness appear to be (i) the endothermicity of hydrogen abstraction, (ii) the absence of long-lived complexes between these molecules and nitrogen atoms (15).

Of the reactants that have been studied so far, ammonia appears to be the only molecule that reacts fast with $N_2\dagger$ and slowly with N atoms. However, the observation of the first property is in large measure due to the second. Of the hydrocarbons studied, methane, ethane, and neopentane are the most inert to active nitrogen. Methane reacts to a significant extent only at such high temperatures that complications due to secondary hydrogen atom reactions obscure the results (15). The ethane and neopentane reactions appear to suffer a change in mechanism in going from low to high temperatures, as inferred from the observed activation energies (15). The simplest explanation seems to be that the low temperature, low activation energy reaction takes place by a mechanism similar to that suggested for ammonia, e.g.

$$N_2\dagger + C_2H_6 \rightarrow C_2H_5 + H + N_2,$$
$$N + C_2H_5 \rightarrow HCN + CH_3 + H,$$
$$N + CH_3 \rightarrow HCN + 2H,$$

and the high temperature, high activation energy reaction by the direct attack of nitrogen atoms.[16]

To explain the formation of secondary products in the fast reactions of other hydrocarbons with active nitrogen, it is necessary to assume (15) that reactions between nitrogen atoms and nitrogen atom – reactant complexes of the type

$$N + N.X \rightarrow N_2 + X^*$$

occur quite readily. The occurrence of these reactions makes it difficult to detect any contribution from the essentially similar reactions of the type

$$N_2\dagger + X \rightarrow N_2 + X^*.$$

In addition to resonance transfers, $N_2\dagger$ molecules might conceivably take part in two types of direct reactions: those that form two molecules of hydrogen cyanide and those that form one molecule of hydrogen cyanide and a nitrogen atom. However, reactions of the type

$$N_2\dagger + C_2H_2 \rightarrow 2HCN + (E + 8) \text{ kcal.},^{17}$$
$$N_2\dagger + C_2H_4 \rightarrow 2HCN + H_2 + (E - 50) \text{ kcal.},$$

where E is the excitation energy of $N_2\dagger$ above the lowest vibrational level, are probably very slow compared with the nitrogen atom reaction; propylene and the butenes preferentially lose only one carbon atom in the primary reaction to yield ethylene and propylene respectively as main products. Since the binding in the highest observed vibrational level of N_2 is tighter than that in

[16]*At sufficiently high temperatures, the ethane reaction becomes fast enough to go to virtual completion in the time spent in the reaction vessel. The limiting yields of HCN obtained agreed reasonably well with Wrede gauge measurements of the N atom concentration.*

[17]*See Ref. 15 for energy values used in calculating heats of reactions.*

Cl_2, both as regards the dissociation energy and the force constant,[18] it might be expected that the activation energy for addition of $N_2\dagger$ to a double bond would be of the same order as that for the addition of molecular halogen, i.e. 20 to 30 kcal. (21).

Simple hydrocarbon radicals are formed as intermediates in many nitrogen atom reactions. Reactions of the type

$$N_2\dagger + CH_3 \rightarrow N + HCN + H_2 + (E-112) \text{ kcal.}$$

will probably be endothermic and should have a significant energy barrier. In addition they are spin disallowed[19] (see below) and should be slow compared with reactions of the type

$$N + CH_3 \rightarrow HCN + 2H + 10 \text{ kcal.}$$

These considerations make it appear unlikely that $N_2\dagger$ molecules would form much hydrogen cyanide by taking part in direct reaction.

THE ROLE OF SPIN CONSERVATION IN NITROGEN ATOM REACTIONS

The possible importance of electron spin conservation in reactions of atomic nitrogen has been suggested by Walsh (67). Nitrogen atoms in the ^4S state have three unpaired electron spins, and several features of the unified mechanisms suggested in a subsequent paper (15) make it appear likely that reactions that conserve spin occur more readily than those that do not.

The theoretical principle of spin conservation (69) says that the total spin of collision partners must remain unchanged before and after collision. The approximation on which it is based is only justified if the interaction between spin and orbital angular momentum is small. It is therefore similar to the prohibition of intercombinations between states of different multiplicities in the spectroscopic selection rules and applies only to light atoms that show Russell–Saunders coupling. The implications of spin conservation can be seen most clearly by the description in terms of potential surfaces given by Laidler and Shuler (41) in an excellent review of reactions involving excited electronic states.

When two molecules with spin vectors S_1 and S_2 approach each other their interaction may be represented by a set of potential surfaces with different spin labels given by the quantum number S where, by the usual vector sum rules, S can have the values

$$S = (S_1+S_2)(S_1+S_2-1)(S_1+S_2-2) \ldots (|S_1-S_2|) .$$

Since the molecules approach at random so far as the direction of their spin vectors is concerned, the relative probability that they interact on a potential surface of spin S will be given by the multiplicity $2S+1$. For a reaction that

[18] *Neglecting anharmonicity, the ratio of the force constants is* $k_{Cl_2}: k_{N_2\dagger} = 0.3$ *and the heats of dissociation are 2.5 ev. and 3.2 ev. for* Cl_2 *and* $N_2\dagger$ *respectively, where the values for* $N_2\dagger$ *have been taken for the highest observed vibrational level of the ground state (28).*

[19] *Spin allowed reactions of the type*

$$N_2\dagger + CH_3 \rightarrow N(^2D) + HCN + H_2 + (E-169) \text{ kcal.}$$

should have a high energy barrier.

reaches completion on a given potential surface, it must be possible to obtain the corresponding value of S from the vector sum of the spin vectors of the products.

It seems likely (15) that a change of spin occurs in many of the reactions of active nitrogen. It is quite important therefore to consider the probability of crossing from one potential surface to another with a change of spin. Estimates of this probability have been made directly from the Landau–Zener equation using values for spin-orbital interaction energy, etc., determined from atomic spectra, and by calculating back from the observed transmission coefficients of reactions in which a change of spin occurs. Laidler and Shuler (41) have reviewed the rather scanty kinetic data and conclude that when a change of spin occurs in reactions involving light atoms the transmission coefficient is probably always less than 10^{-4}. However, direct estimates from spectroscopic data (62) indicate that it might be as high as 0.1. The discrepancy may be explained by partial cancellation of the larger contributions to the interaction energy caused by the rapid precession of orbital angular momenta, etc., (62). However, the accurate evaluation of transmission coefficients requires a high degree of precision in the determination of activation energies and complete faith in the statistical methods of the theory of absolute reaction rates, so that the extent to which such cancellation will occur is uncertain. A lower limit for the probability of a change in spin during collision in systems containing nitrogen may be estimated from the absence of Vegard–Kaplan bands in the spectrum of the afterglow. The radiation lifetime of the $A^3\Sigma$ state is between 10^{-3} and 10^{-4} sec. (47) and it is probably safe to assume that the collision rate between an A molecule and other molecules was less than 10^7/sec. in the spectroscopic studies. Hence, the probability of a change in spin during collision must have been at least 10^{-3} to 10^{-4}.

There are, as yet, no data for nitrogen atom reactions that are sufficiently accurate to permit calculation of transmission coefficients. Long-lived collision complexes are probably formed in several nitrogen atom reactions (15). These can only survive as long as there is a redistribution of the translational energy of the collision among the internal degrees of freedom of the complex. This redistribution should result in a greatly increased chance of crossing from one potential surface to another with a change of spin, since the complex may pass through the critical configuration many times during its lifetime. It is quite possible that, for these reactions, formation of the complexes is rate-determining, so that the kinetics will give no information about restrictions on a change of spin. Nevertheless, nitrogen atom reactions do provide quite good qualitative evidence that there is a restriction on a change in spin.

For example, the mechanism of the reaction of nitrogen atoms with ethylene is probably (15)

$$N + C_2H_4 \rightarrow HCN + CH_3, \qquad [3]$$

$$N + CH_3 \rightarrow HCN + 2H. \qquad [4]$$

Reaction [3] involves a change of spin; the reactants approach on a quartet surface (three unpaired spins) and the products separate on a doublet surface

(one unpaired spin). Reaction [4] conserves spin if the interaction takes place on the triplet surface (vector sum of two unpaired spins). Since interaction can also occur on a quintuplet surface (four unpaired spins), reaction [4] will be spin-allowed for three out of every eight collisions. There is no indication that, although fast (61), the reaction

$$CH_3 + C_2H_4 \rightarrow C_3H_7$$

occurs to any extent in the nitrogen atom reaction with ethylene, even in the presence of excess ethylene. Hence, the reaction [4] must be much faster than reaction [3]. The difference in rate can be explained most easily by a restriction on the required change of spin in reaction [3].

Again, the reaction

$$N + CH_3 \rightarrow HCN + H_2 \qquad [5]$$

is much more favorable energetically than reaction [4], and might be expected to occur preferentially since there is good evidence that movement of hydrogen atoms occurs easily in nitrogen atom reactions (15). However, to explain the observed products of the ethylene and the propylene reactions with active nitrogen, it is necessary to assume that reaction [4] predominates. The most obvious reason for this appears to be that reaction [5] does not conserve spin.

The most plausible mechanism to account for the quite significant amounts of acetylene formed in the ethylene reaction appears to be (15)

$$N + N.C_2H_4 \rightarrow N_2 + C_2H_4^*, \qquad [6]$$

$$C_2H_4^* \rightarrow C_2H_2^* + H_2, \qquad [7]$$

$$C_2H_2^* \rightarrow C_2H_2, \qquad [8]$$

where $C_2H_4^*$ and $C_2H_2^*$ represent ethylene and acetylene in electronically excited triplet states and $N.C_2H_4$ is a collision complex. From quenching experiments with excited metal atoms, reaction [7] is known to occur when the excitation energy is sufficiently high and it has already been pointed out (41) that this is a good example of spin conservation.[20] Reaction [6] would have to compete with the energetically more favorable reaction

$$N + N.C_2H_4 \rightarrow N_2 + C_2H_4. \qquad [9]$$

Both reactions [6] and [9] are spin-allowed. However, reaction [6] should occur three times as often, other things being equal, since it will occur when the original interaction takes place on a triplet surface, while reaction [9] should take place on a singlet surface.

Rather similar mechanisms probably account for the formation of unsaturated hydrocarbons as secondary products of the reactions of both the alkyl halides and the saturated hydrocarbons with active nitrogen (15). The preferential formation of unsaturated hydrocarbons, particularly the formation of acetylene, is very difficult to understand unless spin conservation is important in these reactions.

[20] *Without calling on spin conservation, it is difficult to see how reaction* [7] *could compete with the spin disallowed deactivation reaction*

$$C_2H_4^* \rightarrow C_2H_4.$$

APPENDIX. DEACTIVATION OF VIBRATIONALLY EXCITED NITROGEN MOLECULES

Let M_v be the concentration of excited molecules in the vth vibrational level at time t. Then, on the reasonable assumptions that thermal excitation can be neglected, and that collisions in which only one quantum of energy is transferred are much more likely than those in which several quanta are transferred, the rates of change of the various M_v values with time are given by

$$dM_v/dt = K_{v+1}\,M_{v+1} - k_v M_v, \qquad v = 1, 2, \ldots (n-1), \qquad [I]$$

where n is the highest level excited, and k_v is the rate constant for deactivation of the vth level,
and

$$dM_n/dt = -k_n M_n, \qquad [II]$$

$$dM_0/dt = k_1 M_1. \qquad [III]$$

If, for simplicity, it is assumed that $k_v = k$ for all values of v, and that initially

$$t = 0, \qquad M_n{}^0 = M_n, \qquad M_v = 0 \text{ if } v \neq n,$$

then it can be shown that the solution of equations [I], [II], and [III] is

$$M_{n-j}/M_n{}^0 = x^j e^{-x}/(j!), \qquad j = 0, 1, \ldots (n-1),$$

and

$$M_0/M_n{}^0 = 1 - \sum_{j=0}^{n-1} (M_{n-j}/M_n{}^0)$$

where x stands for kt.

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[21]*A series of papers by Strutt (Lord Rayleigh) in Proc. Roy. Soc., 1911–1922, discuss many interesting observations on active nitrogen.*

CONDUCTANCES OF LITHIUM NITRATE SOLUTIONS IN ETHYL ALCOHOL AND ETHYL ALCOHOL - WATER MIXTURES AT 25.0°C.[1]

By A. N. Campbell and G. H. Debus[2]

ABSTRACT

The conductances of solutions of lithium nitrate in 30, 70, and 100 weight per cent ethyl alcohol have been determined at concentrations ranging from 0.01 molar up to saturation, at 25°C. The densities and viscosities of these solutions have also been determined. The data have been compared with the calculated conductances obtained from the Wishaw–Stokes equation. The agreement is fairly good up to, say, 2 *M*, for all solvents except absolute alcohol. In the latter solvent there is no value of å, the distance of closest approach, which will give consistent values of the equivalent conductance. In passing from pure water to pure alcohol, the value of å increases progressively and this we attribute to a change in the solvation of the lithium ion from water molecules to alcohol molecules. Some further calculations incline us to the view that the nitrate ion, as well as the lithium ion, is solvated to some extent, at least in alcohol.

The work of this laboratory for several years past has been directed to the determination of the electrical conductances of concentrated aqueous solutions of various electrolytes (4). More recently we have compared our experimental results with those calculated by means of the Wishaw–Stokes equation (10). The agreement between calculated and observed values, though far from exact, has nevertheless been sufficiently close to be very striking, so much so that we are convinced that the quantity å, the "distance of closest approach", is a real quantity, at least in so far as such theoretical concepts can ever be considered real. The constant occurrence of this quantity in expressions for the calculation of activity coefficients also lends support to this view, although the numerical values obtained by the two methods do not often agree with another.

The remaining quantity introduced into the Wishaw–Stokes equation, viz., the relative viscosity, is less satisfactory. Unquestionably, an ion moves less rapidly in a more viscous medium but the precise nature of the resistance to its motion is rather indefinite and certainly it is not measured quantitatively by the bulk viscosity. The approximate agreement between observed and calculated results, however, shows that, in most cases, the bulk viscosity is an approximation to the truth.

The vexed question of viscosity can be avoided by confining investigation to solutions whose viscosity does not differ greatly from that of the solvent; such solutions are not necessarily dilute. When, under such conditions, the observed (equivalent) conductance is found to be less than the calculated, Robinson and Stokes (8) attribute this to ion-pair formation, and they have had some success in the calculation of an ionization constant.

[1]*Manuscript received May 14, 1956.*
Contribution from the Chemistry Department of the University of Manitoba, Winnipeg, Manitoba.
[2]*National Research Council of Canada Postdoctorate Fellow.*

In our work on the conductance of aqueous lithium nitrate solutions, the agreement between calculated and observed conductance remains good up to the very high concentration of 6 *M*. This we attributed to the absence of ion-pairs and this again could be very well accounted for as due to the complete insulation of the lithium ion by its firmly bound water of hydration. We presumed, however, that if we added alcohol, in increasing amounts, this would have the dual effect of stripping water from the hydration sheath and of lowering the dielectric constant and both these effects would tend to favor ion-pair formation. We expected, therefore, that at a rather sharply defined alcohol concentration deviation would commence between the calculated curve of conductance and the observed one, in the direction of the observed becoming less than the calculated. It was on this basis that the present work was undertaken. It should be said at once that none of these expectations has been realized and that the behavior of lithium nitrate solutions in alcohol and alcohol–water mixtures requires a totally different explanation.

EXPERIMENTAL

Our technique for conductance and viscosity determinations has been described elsewhere (4). Solvents consisting of 30 and 70 weight per cent alcohol were obtained by diluting a commercial 95% ethyl alcohol, which had been purified by distillation from freshly ignited lime. A sufficient volume of each solvent to complete the series of measurements was made up and stoppered off. For absolute alcohol as a solvent, a so-called "absolute" alcohol, obtained from Canadian Industrial Alcohols and Chemical Limited ("Guaranteed to meet the Specifications of the British and U.S. Pharmacopoeia"), was treated with magnesium ethoxide and distilled through a Podbelniak column. The alcohol content of the solvents was checked by density and dielectric constant determinations. The latter, extrapolated to zero frequency, were found to be in good agreement with those of Åkerlöf (1). Measurements of conductance, density, and viscosity of solutions in absolute alcohol were all made in stoppered vessels since absolute alcohol is notoriously hygroscopic. This precaution was not necessary with the diluted alcohols.

EXPERIMENTAL RESULTS

The B, B_1, and B_2 values of the Wishaw–Stokes equation are calculated for each solvent, from the viscosity, dielectric constant, and temperature, and are given at the head of each table. Our results, both observed and calculated, are contained in Tables I, II, and III. In Figs. 1, 2, and 3, the equivalent conductances, observed and calculated for the most favorable value of å (see Table IV), are plotted against molar concentration. Fig. 4 represents similar results obtained by Klochko and Grigorjew (7) for lithium nitrate in methyl alcohol, and calculated by us in the same way.

DISCUSSION OF RESULTS

The viscosity of ethyl alcohol – water mixtures is anomalous. The results of Bingham and Jackson (3) show a maximum viscosity at about 50% alcohol, where the mixture is 2.685 times as viscous as water and 2.189 times as viscous

TABLE I

$LiNO_3$ IN 30% C_2H_5OH+70% H_2O, T = 25.00°C.
B_1 = 0.3333, B_2 = 28.04, B = 0.3726

Wt. % $LiNO_3$	C, mol./l.	$d_4^{25°}$	η/η_0	$\kappa\times10^4$	Λ_{exp}	$\Delta\eta/\eta_0$	Λ_{calc}			
							$\mathring{a}$ = 4	$\mathring{a}$ = 4.5	$\mathring{a}$ = 5	$\mathring{a}$ = 6
0	0	0.9507	1.000	—	—	—	51.5†	51.5†	49.50	48.0
0.1370	0.01891	0.9516	1.001	819.3*	43.34	43.38	—	46.47	—	43.35
0.3080	0.04256	0.9526	1.002	1801.0*	42.32	42.40	—	44.57	—	41.74
0.6230	0.08623	0.9543	1.004	3471.8*	40.26	40.42	—	42.58	—	40.06
3.711	0.5231	0.9720	1.033	18711	35.77	36.59	35.30	36.01	34.47	34.37
7.359	1.059	0.9920	1.073	32726	31.91	32.83	30.62	31.85	—	30.75
11.967	1.769	1.019	1.128	47925	27.10	30.27	27.24	28.53	27.91	28.14
15.013	2.259	1.038	1.187	55911	24.74	29.09	24.97	26.26	—	25.94
19.327	2.985	1.065	1.288	64403	21.57	27.50	22.06	23.27	22.80	23.03
24.727	3.951	1.102	1.472	70553	17.86	26.04	18.40	19.42	—	19.21
27.958	4.561	1.125	1.613	71798	15.74	25.14	16.33	17.14	16.93	17.03
28.565	4.680	1.130	1.665	71780	15.33	25.03	—	16.62	—	16.42
33.37	5.643	1.166	1.968	70558	12.51	24.38	—	13.54	13.23	13.25
38.04	6.639	1.203	2.445	67439	10.16	24.60	—	10.46	—	10.18
43.33	7.850	1.249	3.226	61885	7.88	25.17	—	7.55	—	7.24‡
48.79	9.188	1.298	4.450	55222	6.01	26.74	—	5.14	—	4.88‡
53.66	10.48	1.347	6.48	48498	4.63	30.00	—	3.38	—	3.13‡
54.15	10.62	1.352	6.77	47837	4.51	30.53	—	3.22	—	2.98‡

*Corrected for solvent.
†Whitman and Hurt's value of Λ_0.
‡$\kappa\mathring{a}_{max} = 6$.

TABLE II

$LiNO_3$ IN 70% C_2H_5OH+30% H_2O, T = 25.00°C.
B_1 = 0.6798, B_2 = 38.05, B = 0.4724

Wt. % $LiNO_3$	C, mol./l.	$d_4^{25°}$	η/η_0	$\kappa\times10^4$	Λ_{exp}	$\Delta\eta/\eta_0$	Λ_{calc}		
							$\mathring{a}$ = 6.5	$\mathring{a}$ = 7.5	$\mathring{a}$ = 8.5
0	0	0.8634	1.000	—	—	—	37.20	36.7	36.4
0.0903	0.01132	0.8640	1.004	364.9*	32.23	32.59	32.07	31.76	31.75
0.1981	0.02484	0.8644	1.009	753.6*	30.30	30.57	30.32	30.12	29.98
0.6823	0.08582	0.8672	1.029	2290.4	26.69	27.46	26.76	26.89	26.85
1.009	0.1271	0.8691	1.043	3244.6	25.54	26.64	25.44	25.62	25.63
1.908	0.2419	0.8740	1.073	5629	23.28	24.98	23.05	23.41	23.49
4.274	0.5502	0.8877	1.160	10763	19.56	22.69	19.24	19.69	19.82
6.378	0.8324	0.8999	1.250	14409	17.31	21.64	16.76	17.31	17.42
9.484	1.263	0.9182	1.386	18557	14.69	20.36	13.98	14.39	14.67
12.78	1.740	0.9384	1.579	21487	12.35	19.50	11.38	11.68	11.72
16.99	2.379	0.9654	1.875	23588	9.91	18.58	8.68	8.80	8.79
19.54	2.785	0.9822	2.108	24080	8.65	18.23	7.24	7.29	7.23†
23.92	3.510	1.012	2.610	23917	6.81	17.74	5.17	5.18†	5.12†
28.51	4.324	1.045	3.359	22751	5.26	17.67	3.46†	3.39†	3.35†
32.31	5.034	1.074	4.194	21503	4.19	17.57	2.41†	2.37†	2.36†
37.22	6.012	1.113	5.723	19605	3.26	18.66	1.46†	1.43†	1.42†

*Corrected for solvent.
†$\kappa\mathring{a}_{max} = 6$.

as alcohol. This behavior indicates an interaction between the components of the mixture which is unfortunate for the purpose of this investigation.

In order to use the Wishaw–Stokes equation, it is necessary to know the value of Λ_0, and this is usually not known for temperatures other than 25° and for solvents other than water. For pure alcohol, we fortunately possess some very

TABLE III

$LiNO_3$ IN C_2H_5OH AT 25.00°C.
$B_1 = 1.330$, $B_2 = 89.91$, $B = 0.5908$

Wt. % $LiNO_3$	C, mol./l.	$d_4^{25°}$	η/η_0	$\kappa \times 10^6$	Λ_{exp}	$\Delta\eta/\eta_0$	Λ_{calc}				
							å = 2	å = 4	å = 6	å = 8	å = 10
0	0	0.7850	1.000	—	42.7*	42.7	42.7	42.7	42.7	42.7	42.7
—	0.000219	—	—	—	40.25*	—	40.63	—	—	40.74	40.75
—	0.001285	—	—	—	36.52*	—	37.78	—	—	38.27	38.62
—	0.002407	—	—	—	34.39*	—	36.11	36.85	36.72	26.97	37.21
2.158	0.2503	0.7997	1.276	3073.5	12.28	15.67	6.10	—	—	16.22	17.46
4.500	0.5321	0.8154	1.591	4824.7	9.07	14.43	—	7.43	9.11	9.16	—
7.457	0.9916	0.8399	2.209	6437.1	6.49	14.34	—	3.18	5.09	6.09	—
12.43	1.567	0.8689	3.215	7325.3	4.68	15.05	Negat.	—	—	2.89†	—
16.33	2.121	0.8958	4.365	7534.6	3.55	15.50	Negat.	0.73	1.29†	1.22†	—
19.49	2.593	0.9174	5.617	7387.3	2.85	16.01	Negat.	0.40†	0.64†	0.64†	—
23.39	3.206	0.9450	7.51	7114.5	2.22	16.67	Negat.	0.15†	0.19†	0.19†	—

*Copley, Murray-Rust, and Hartley (6).
†$\kappa å_{max} = 6$.

TABLE IV

MOST FAVORABLE VALUES OF å

Solvent	å in Angstroms
Water	4.5
30% alcohol	6.0
70% alcohol	7.5 to 8.5
100% alcohol	No value gives consistent results

accurate conductance figures for dilute solutions of lithium nitrate, due to Copley, Murray-Rust and Hartley (6), and by treating these figures in the usual way we arrived at 42.7 mhos as the value of Λ_0 in alcohol at 25° C. For 30% alcohol, figures are available by Whitman and Hurt (9), which yield 51.5 mhos as the value of Λ_0. Our own figures for the relatively high concentrations of 0.01891, 0.04256, and 0.08623 N gave $\Lambda_0 = 48.5 \pm 1.0$ mhos, and this value fits the Wishaw–Stokes equation better than the higher figure; we have used 49.5 and 48.0 in calculation. For 70% alcohol we used our own data for solutions of 0.01132, 0.02484, and 0.08582 N, and from these we estimate Λ_0 as 36.7 ± 1 mhos; we have calculated with 37.20, 36.7, and 36.4. However, none of these Λ_0 values has any great accuracy and they must be considered as semiempirical parameters. It is not surprising that Λ_0 in 70% alcohol should be less than Λ_0 for pure alcohol, since this solvent is more viscous than pure alcohol, but the fact that the 70% solvent shows a lower Λ_0 than 30% alcohol cannot be explained purely on the grounds of viscosity, since the 30% alcohol is slightly more viscous than the 70% mixture. It seems obvious to us, from this and other observations, that the solvation sheath of the lithium ion changes from a predominantly water sheath to a predominantly alcohol sheath, between 30 and 70% alcohol.

A recent treatment by Amis (2), however, would seem to indicate that this deduction is not inevitable, in other words, that the occurrence of a minimum

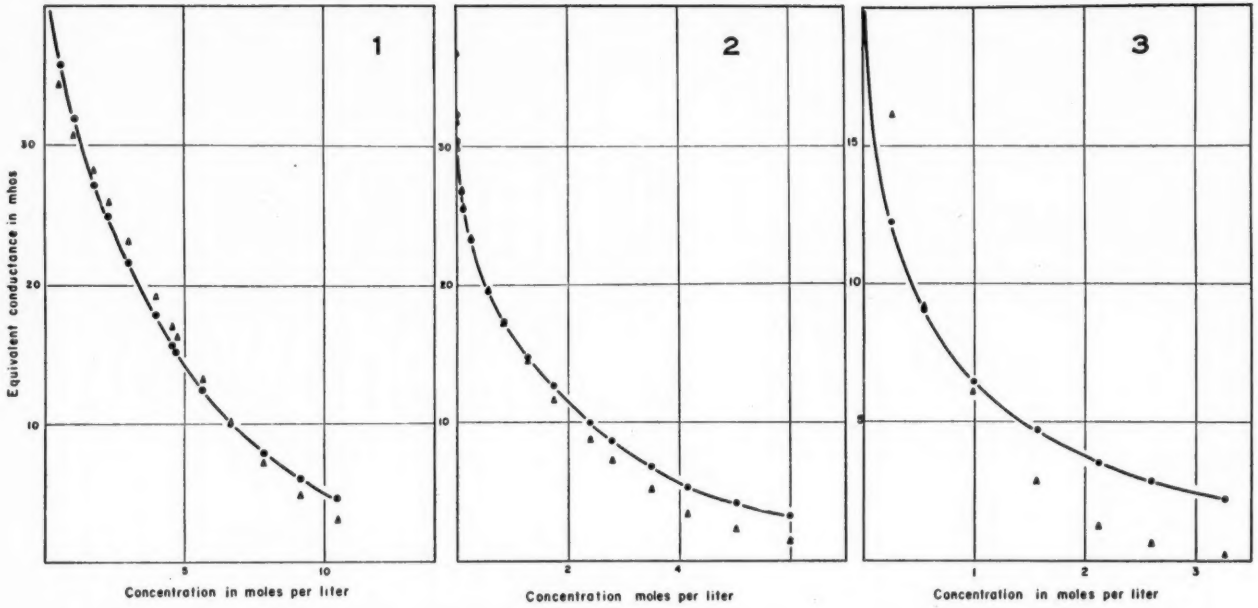

FIG. 1. $LiNO_3$ at 25.00°C. Solvent: 70 wt-% H_2O, 30 wt-% C_2H_5OH. ● Experimental values. △ Calculated values; å = 6, A_0 = 48.
FIG. 2. $LiNO_3$ at 25.00°C. Solvent: 30 wt-% H_2O, 70 wt-% C_2H_5OH. ● Experimental values. △ Calculated values; å = 7.5, A_0 = 36.7.
FIG. 3. $LiNO_3$ at 25.00°C. Solvent: C_2H_5OH. ● Experimental values. △ Calculated values; å = 8, A_0 = 42.7.

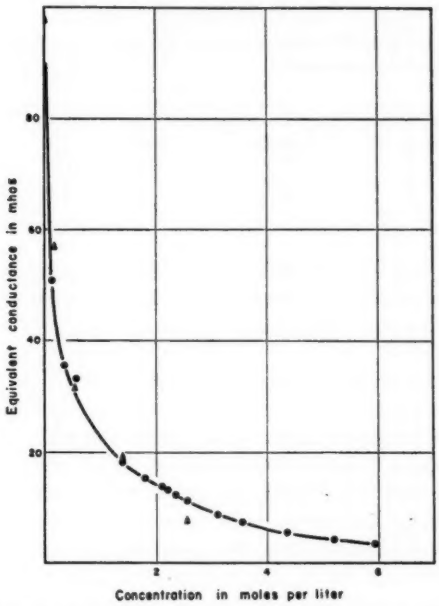

FIG. 4. $LiNO_3$ at 25.00°C. Solvent: CH_3OH. ● Experimental values. △ Calculated values; å = 8, Λ_∞ = 98. Results of M. A. Klochko and I. G. Grigorjew.

value of Λ_0, when Λ_0 is plotted against alcoholic content, may be merely a consequence of changes in viscosity, dipole moment, and dielectric constant. Amis gives the formula:

[1] $$\frac{\Lambda_0 \eta \mu}{D} = \text{constant}$$

where μ and D mean the dipole moment and dielectric constant, respectively. It is assumed that the dipole moment of a mixed solvent can be calculated by the mixture rule from the dipole moments of the constituents, thus:

[2] $$\mu = N_1\mu_1 + N_2\mu_2.$$

Since the dipole moments of water and of alcohol differ only slightly, the calculation is a very reasonable one, in this case. Using the unexceptionable data for Λ_0 in pure water, we obtain for the constant the value 0.023046, and using this constant we obtain Table V.

The figures for Λ_0 are far from agreeing but the calculated values show the same minimum as do the observed.

When considering the increase in å in passing from water to alcohol (see Tables I, II, and III), it seems natural to attribute this entirely to a change in lithium ion solvation but some afterthoughts incline us to think that the NO_3^- ion may not be as bare and unchanging as is sometimes supposed. The fol-

TABLE V

Λ_0, OBSERVED AND CALCULATED, FOR MIXTURES OF ETHYL ALCOHOL AND WATER, AT 25°C.

Wt. % ethyl alcohol	D	η	μ	$\Lambda_{0_{calc}}$	$\Lambda_{0_{obs}}$
0.00	78.5	0.00893	1.84	—	110.1
30.00	61.1	0.0218	1.83	37.77	48.0
70.00	38.0	0.02037	1.77	24.29	36.7
100.00	24.3	0.0109	1.70	30.22	42.7

lowing formula, given by Robinson and Stokes (8), is derived on the assumption that the Stokes' viscosity law applies to the motion of an ion:

[3] $$r = (0.820 \mid Z \mid/\lambda^\circ\eta_0)(r/r_s) .$$

In this formula, r is the radius of the ion in solution, r_s is the so-called "Stokes radius", i.e. the radius if Stokes' law were rigorously obeyed, and λ° the limiting ionic conductance. Thus, (r/r_s) is an empirical correction factor depending on the value of r_s, designed to bring the Stokes' radius into line with that calculated by other methods. If it is assumed that the radius of the nitrate remains constant (no solvation) and that the correction factor remains the same in solvents other than water, we have the relation

[4] $$\lambda^\circ \propto 1/\eta_0.$$

Equation [4] is none other than Walden's rule, which is actually valid in many cases. Hence, knowing λ° in pure water at 25° C. (71.46 mhos for NO_3^- ion) it is possible to calculate λ° for NO_3^- ion in other solvents and hence by subtraction from Λ_0 to obtain λ° for Li^+ ion. The results are contained in Table VI.

TABLE VI

IONIC CONDUCTANCES IN VARIOUS CONCENTRATIONS OF ALCOHOL

Wt. % alcohol	$\lambda^\circ_{NO_3^-}$	$\Lambda_{0_{exp}}$	$\lambda^\circ_{Li^+}$
0.00	71.46	110.1	28.68
30.00	29.27	48.0	18.73
70.00	31.32	36.7	5.38
100.0	58.54	42.7	−15.84

The negative value for $\lambda^\circ_{Li^+}$ in alcohol is impossible and this implies either that Equation [3] is incorrect in its application to water–alcohol mixtures or that the assumption of a constant radius for the nitrate ion is untenable, or that the correction factor is not constant.

Using the values of $\lambda^\circ_{Li^+}$ listed in Table VI, r_{Li^+} is now calculated from Equation [3], while $r_{NO_3^-}$ is calculated from the water data. There is some uncertainty about the latter value, since the correction factor (r/r_s) is large. The calculation is impossible for pure alcohol since $\lambda^\circ_{Li^+}$ has a negative value (Table VI). The results are collected in Table VII.

For the three solvents of Table VII, it might be assumed that the difference

TABLE VII

EFFECTIVE RADII IN SOLUTION OF Li^+ AND NO_3^- IONS

Wt. % alcohol	Radii in solution, Å		$r_{NO_3^-}+r_{Li^+}$, Å	å from Stokes' equation, Å
	Li^+	NO_3^-		
0.00	3.7	3.0	6.7	4.5
30.0	3.4	3.0	6.4	6.0
70.0	7.5	3.0	10.5	7.5

between å and $r_{Li^+}+r_{NO_3^-}$ represented "penetration" but, since absolute alcohol yields an impossible result, we consider it more likely that the fallacy lies in assuming the NO_3^- ion has a constant radius irrespective of the solvent. If it is admitted that the nitrate ion is solvated like the lithium ion, though not to the same extent, we have an obvious explanation of the failure of theory to agree with experiment.

In the two aqueous alcohols the agreement with the Wishaw–Stokes equation is good up to 2 *M*, using for å the value 6.0 in 30% alcohol, and 7.5 in 70% alcohol. No assigned value of å, however, gives good results in pure alcohol. We have used the value å = 8.0, but reference to Table III will show that all values of å are equally unsatisfactory. For solutions in pure water we previously used å = 4.5 and obtained excellent agreement (5). We have alluded in the introduction to the somewhat doubtful nature of the viscosity correction

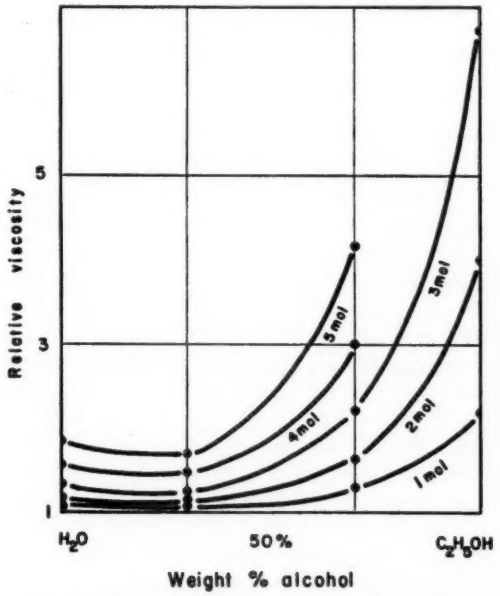

FIG. 5. Relative viscosity vs. weight per cent alcohol in the solvent.

and we see in this a possible explanation of the anomalous behavior of solutions in anhydrous alcohol. Fig. 5 is intended to illustrate this point. In this figure, the relative viscosity, that is to say the viscosity of the solution divided by the viscosity of the solvent, is plotted for interpolated concentrations of 1, 2, 3, 4, and 5 molar, against weight per cent alcohol in the solvent. It will be observed that the relative viscosity increases enormously at the higher alcohol concentrations; thus, a 3 *M* solution in absolute alcohol is seven times as viscous as the solvent, while in 70% alcohol it is only about twice as viscous. It may be that at these very high relative viscosities, the simple expedient of dividing the calculated equivalent conductance by the relative viscosity is no longer a permissible approximation.

In Fig. 6 the (observed) specific conductance is plotted against molar

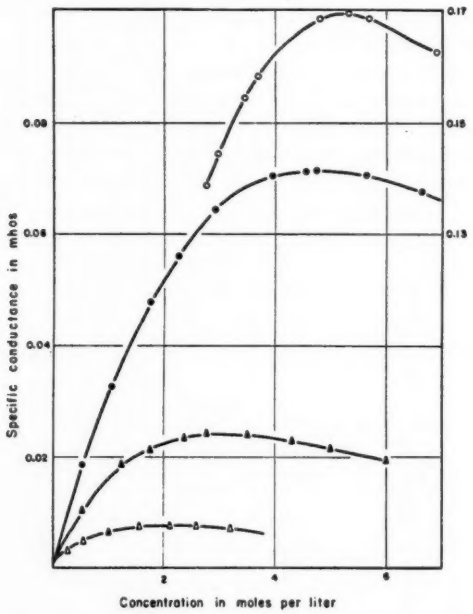

FIG. 6. $LiNO_3$. ○ H_2O. ● 70% H_2O+30% C_2H_5OH. ▲ 30% H_2O+70% C_2H_5OH. △ C_2H_5OH.

concentration for pure water and the three alcoholic solutions. In all four cases, the specific conductance passes through a maximum. The concentration at which the maximum occurs decreases as we pass from pure water to pure alcohol; the curve also becomes much flatter. The maximum occurs at (approximately) 5 *M* for pure water, at 2 *M* for pure alcohol, and at intermediate molarities for intermediate strengths of alcohol.

As usual in our work, we have plotted in Fig. 7 Λ_0 against log c, and obtained

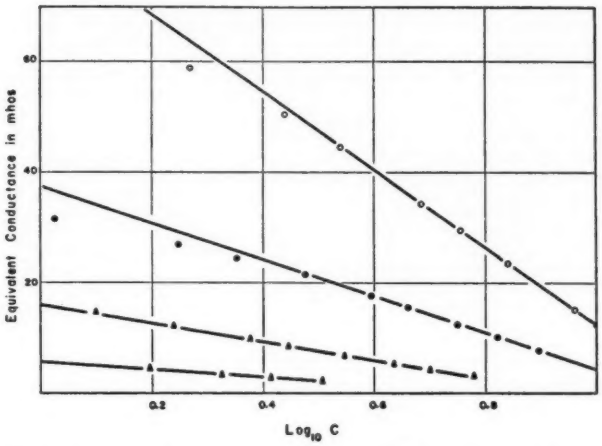

FIG. 7. ○ H_2O. ● 70% H_2O+30% C_2H_5OH. ▲ 30% H_2O+70% C_2H_5OH. △ C_2H_5OH.

the usual straight line. There is no theoretical justification for doing this and it may be contended that any function plotted logarithmically will give a straight line; admittedly, the variation is reduced by this procedure. We still think, however, that this explanation is a little too facile for a relationship which we have hardly ever found to fail.

The main conclusion of this work is that, despite the lowered dielectric constant in alcohol and alcohol–water mixture, lithium nitrate solutions do not form ion-pairs in these solvents. If the å values used by us in the calculations of Λ are accepted as having real physical significance, our deduction receives immediate support; with these very large distances of closest approach, the ions can never get close enough for ion-pair formation, despite the fact that this minimum distance is increased by the reduced dielectric constant. The increase in the distance of closest approach is explained as due to a change of the solvation sheath from water to alcohol molecules. We attempted a direct experimental confirmation of this by determining the (short wave) infrared absorption of solutions of lithium nitrate in water and in alcohol but, over the range of wave-length available to us, we could detect no difference in the vibration frequencies of the OH-group or its first two harmonics. This, of course, is no argument against the occurrence of solvated complexes since, if attachment is at the hydroxylic oxygen, as it presumably is, this would scarcely alter the frequency, since the hydrogen atom is so much lighter than the oxygen atom in any case.

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A DILATOMETRIC STUDY OF SOLID METHANOL-*d*[1]

By D. W. Davidson

ABSTRACT

With isopentane as the dilatometric liquid, CH_3OD was examined between 120°K. and the melting point. There is evidence of two transitions within the solid: one, in the vicinity of 158°K., appears to be a gradual transition, the other, at 163°K., a first-order one. The corresponding molar volume changes are 0.04 and 0.43 ml. A further change of volume of 2.67 ml./mole occurs at the melting point. These results are compared with recent dilatometric results for CH_3OH and discussed with reference to the available calorimetric data. The molar volume of CH_3OD is slightly greater than that of CH_3OH in both liquid and solid forms.

The presence of a phase transition within solid methanol has been known for some time (4, 5). Recently the nature of the transition has been investigated in a number of studies on solid methanol in which a variety of experimental approaches has been used. These have included a new calorimetric study by Staveley and Gupta (6), an X-ray examination of the low and high temperature modifications of the solid by Tauer and Lipscomb (8), and an investigation by Cooke and Drain (1) of the proton magnetic resonance line width. In a recent dilatometric study of CH_3OH, Staveley and Hogg (7) found evidence of *two* transitions only a few degrees apart. As long as the presence of only one transition had been assumed, it had usually been classified as a λ-type transition, rather than a first-order one, largely as a result of heat capacity measurements. Thus, when the sample was heated through the transition, thermal equilibrium was rapidly reached in the early stages of the transition but only slowly in the later stages (6). Now it appeared that the thermal measurements had included contributions from two distinct transitions: one apparently a gradual, non-isothermal transition occurring in the vicinity of 156°K., the second, at 159°K., probably a typical first-order transition at which the change from the monoclinic to orthorhombic structure (8) took place.

The calorimetric study by Stavely and Gupta (6) appears to be the only published work on CH_3OD. The thermal behavior of CH_3OD in the vicinity of the heat capacity maximum showed the same anomalies as it did for CH_3OH. This suggests that there are two transitions in CH_3OD as well.

The present work was undertaken to check this possibility and, if possible, to throw some light on the nature of the lower temperature, gradual transition.

EXPERIMENTAL

The thermostat consisted of a heater-wound aluminum block, insulated and placed in a copper can which was mounted in a 5-gal. Dewar flask. Liquid nitrogen was admitted to the latter to a height kept roughly constant by a bimetallic thermoregulator with its tip just immersed in the nitrogen. This

[1]*Manuscript received June 5, 1956.*
Contribution from the Division of Applied Chemistry, National Research Council, Ottawa, Canada. Issued as N.R.C. No. 4037.

regulator controlled the compressed air supply which intermittently supplied liquid nitrogen from an external tank. A second regulator, mounted in the block, controlled the heater circuit. Temperature was measured by two copper–constantan thermocouples, one in the central air cavity of the block and one in the block itself. These thermocouples were calibrated by the Applied Physics Division of N.R.C. to an absolute accuracy of $\pm 0.2°$. A period of at least two hours was allowed for temperature equilibration after the thermostat had been set for a new temperature. In the region of the transitions a period of about five hours was allowed.

Because of the tendency of methanol to shatter the containing bulb when the solid is warmed, a carrot-shaped dilatometer bulb was used as an alternative to the method of Staveley and Hogg (7), who placed the sample in a separate loose tube within the dilatometer bulb. No shattering was encountered. A 1 meter length of calibrated 1 mm. capillary tubing was sealed to the large end of the bulb.

The dilatometric fluid was isopentane (Phillips Petroleum Co., 99 mole% minimum) which was distilled over calcium hydride; a middle fraction was used. The known densities of isopentane (2) were extended to the lowest temperature required by following the change of volume of isopentane itself in the dilatometer.

The CH_3OD used contained less than 0.07% by volume of water, as determined by the Fischer reagent. Its infrared spectrum showed less than 1% CH_3OH. A quartz pycnometer of the type described by Kirshenbaum (3) in connection with studies of the density of D_2O, but of smaller (11 ml.) capacity, was constructed for the density determination. The value obtained ($d_4^{20} = 0.81252$) is a little lower than the value reported by Staveley and Gupta (6) (0.81269). Within the accuracy of the refractometer (~ 0.0002), the refractive index (n_D^{20}) was found to be identical with that of CH_3OH.

Like CH_3OH, CH_3OD readily supercools below the main transition temperature. To ensure the complete absence of the orthorhombic form at temperatures below this transition point, a thermal conditioning procedure similar to that used by Staveley and Hogg (7) was followed. All measurements were made with increasing temperature except for occasional tests of reversibility, particularly in the transition regions.

RESULTS

In Fig. 1 the molar volume of CH_3OD is plotted against temperature. The change in volume on melting is only slightly less for CH_3OD than for CH_3OH (see Table I). Both of these volume changes at melting were measured in the presence of isopentane, which is soluble in liquid methanol to the extent of about 1 mole % (7). This accounts for the lowering of the melting point, which is about a degree lower than the value 173.5$_2$°K. reported by Staveley and Gupta (6). A cooling curve run on CH_3OD itself gave a freezing point of 173.6°K.

The principal transition within the solid occurs at 163°K., some four degrees higher than in light methanol. The volume change is 0.43 ml./mole, again

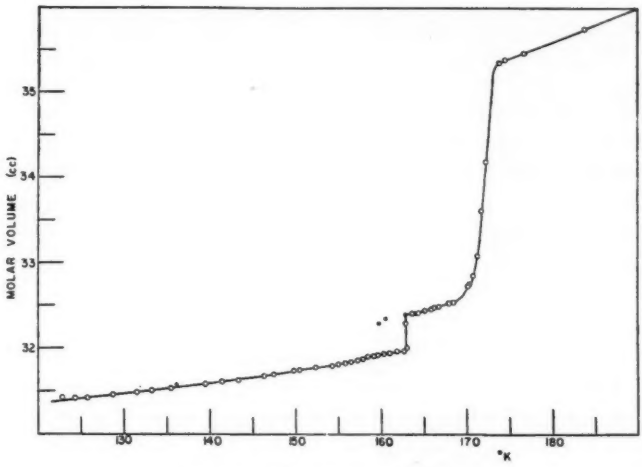

FIG. 1. Molar volume of CH_3OD.

TABLE I

	CH_3OH			CH_3OD		
	$\alpha-\alpha^1$	$\alpha^1-\beta$	Melting	$\alpha-\alpha^1$	$\alpha^1-\beta$	Melting
(*a*) Transition temperatures (°K.)						
Dilatometric method	156	159	—	158	163	(173.6)
Calorimetric method	157.8		175.4	161.1		173.5
(*b*) Molar volume changes (ml.)						
Dilatometric method	~0.14	0.49	2.75	~0.04	0.43	2.67
(*c*) Molar entropy changes (e.u.)						
Calorimetric method	1.08		4.31	0.97		4.18
(*d*) Ratio (*b*): (*c*) (ml./e.u.)		0.45*	0.638		0.44*	0.639

**See text.*

lower than in CH_3OH (0.49). As indicated by the solid circles in Fig. 1, which are volumes obtained with cooling, the high temperature form readily supercools through this transition temperature.

A further change in volume (shown more clearly in Fig. 2) occurs in the vicinity of 158°K., two degrees higher than the gradual transition in CH_3OH. This transition in CH_3OD also appears to be a gradual one. The volume change appears with both increasing and decreasing temperature (the open and filled circles refer to increasing, the crosses to decreasing, temperature) with no sign of supercooling or hysteresis. The volume change (~0.04 ml./mole) accompanying this transition in CH_3OD is very small, even in comparison with the volume change near 156° in CH_3OH (~0.14 ml./mole).

In Table I the present dilatometric results are summarized and compared

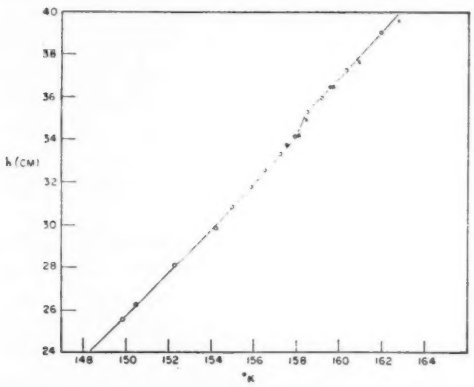

FIG. 2. Height of isopentane column vs. temperature in the region of the low temperature transition.

with the dilatometric data of Staveley and Hogg (7) and the calorimetric results of Staveley and Gupta (6). The low and high temperature transitions are called $\alpha-\alpha^1$ and $\alpha^1-\beta$ transitions respectively.

DISCUSSION

As far as the author is aware, no X-ray study of CH_3OD has yet been made. The similarity of CH_3OD to CH_3OH in its calorimetric and volumetric properties makes it likely that the transition at 163°K. corresponds to a change in crystal form from the monoclinic to the orthorhombic modification; the dimensions of the unit cells in the two modifications are probably not much different from the values given by Tauer and Lipscomb (8) for CH_3OH.

The smallness of the change in volume at the low temperature transition makes it difficult to establish whether or not the transition ends abruptly on the high temperature side. It does, however, appear to set in gradually at least two degrees below the temperature at which the coefficient of expansion reaches its maximum value (158°K.).

The ratios of the molar volume to the molar entropy changes at the melting point and at the first-order $\alpha^1-\beta$ transition are included in Table I. For the melting process this quantity is, within experimental error, the same for both methanol molecules. Since this ratio is a measure of the effect of pressure on the temperature of a first-order transition, this result provides additional evidence for the similarity in the crystal structure of the high temperature forms, and, incidentally, provides a consistency test for the four sets of experimental data.

In the case of the transitions within the solid, it is uncertain what fraction of the total entropy change should be assigned to each of the two transitions. It is apparent, however, that most of this entropy change should be assigned to the first-order $\alpha^1-\beta$ transition. If the whole of the entropy change is so assigned, the result is again that the volume to entropy ratios for the two

molecules are the same. This result is also obtained if the same fraction of the total entropy change is assigned to the $\alpha-\alpha^1$ transitions in both molecules, but the large difference between the volume changes of the two molecules at this transition would seem to make this procedure of doubtful validity. It is difficult to avoid the conclusion that the entropy change at the $\alpha-\alpha^1$ transition is extremely small, perhaps no more than a few one-hundredths of an entropy unit.

The molar volume of CH_3OD is consistently larger than that of CH_3OH (Table II). In the liquid the ratio of molar volumes (1.0046 at 20°) is the same

TABLE II

MOLAR VOLUMES (ML.)

	Liquid (20°C.)	β-Solid (−110°C.)	α-Solid (−160°C.)
CH_3OH, dilatometric	40.488	32.25	30.96
CH_3OD, dilatometric	40.675	32.40	31.27
CH_3OH, X-ray		32.96±0.33	31.41±0.53
Ratio CH_3OD: CH_3OH	1.0046	1.005	1.010
Ratio D_2O: H_2O	1.0036 (25°C.)	1.0016 (0°C.)	

order of magnitude as this ratio for heavy and light water (1.0036 at 25°C.) (3) and the explanation is probably the same, i.e., slightly more regular hydrogen bonding exists in the deuterium-substituted liquid. Values of the molar volumes are also given for the two temperatures in the solid state at which Tauer and Lipscomb did their X-ray work. The dilatometric volumes are smaller than those calculated from the unit cell dimensions but the difference may not be sufficiently great to lie outside the limits of accuracy of the X-ray results.

The greater molar volume of CH_3OD in the solid is particularly evident in the α phase where the difference between the two methanol molecules amounts to 1%. The relatively large molar volume of methanol-*d* in this phase may account for the relatively small volume change at the $\alpha-\alpha^1$ transition. It may be that the lattice is sufficiently expanded in the α-modification that, as the transition region is approached, the further expansion that takes place to accommodate the transition need only be small.

Staveley and Hogg (7) have advanced the suggestion that the gradual transition in CH_3OH may be connected with the disappearance of an alternation in the positions of the methyl groups in planes parallel to the (010) face of the monoclinic crystal. This alternation had been proposed by Tauer and Lipscomb to explain the presence of faint "superlattice" lines in the X-ray pattern at −160°C. The results of the present work on CH_3OD are not inconsistent with this explanation. The small effect of deuterium substitution in the hydroxyl group on the transition temperature suggests that the hydroxyl group may not play an important part in the transition process.

The existence of the second transition in methanol and methanol-*d* is confirmed by recent dielectric work (9). There is a small, but well-defined, rise in

the dielectric constant, as measured at radio frequencies, in the temperature region where the volume change occurs. This effect is particularly pronounced in CH_3OD.

ACKNOWLEDGMENTS

The author is indebted to Dr. L. C. Leitch for supplying the methanol-*d* and to Dr. I. E. Puddington for helpful discussions.

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DEUTERIUM MIGRATION DURING THE IONIZATION OF 1-BUTENE-4-d_3 BY ELECTRON IMPACT[1,2]

By W. A. Bryce and Paul Kebarle

ABSTRACT

The mass spectrum of $CD_3—CH_2—CH=CH_2$ has been measured in a 90° Nier-type mass spectrometer using 50-volt electrons. High resolution nuclear magnetic resonance measurements showed that the methyl group was fully deuterated and that there were no D-atoms located elsewhere in the molecule. This result was supported by infrared analysis. A comparison of the mass spectrum with that of $CH_3—CH_2—CH=CH_2$ shows that the total intensities of each group of C_4, C_3, C_2, and C_1 fragments are the same for both compounds. This indicates equal probabilities of C—C bond rupture in the dissociation of the corresponding parent ions. The distribution of fragments within the groups in the deuterated compound shows, however, that extensive migration of the D-atoms has occurred during ionization. Migration is also evident at much lower electron energies (approximately 15 ev.). The thermal cracking patterns of the two compounds, as determined by gas chromatographic analyses, are very similar.

INTRODUCTION

Migration of hydrogen atoms along the carbon skeleton in ionized hydrocarbon molecules has been proposed to account for the appearance of such fragments as CH_4^+ in the mass spectrum of propane and CH_3^+ in the spectrum of cyclohexane. These peaks can not be accounted for by isotopic contributions from C^{13}. Evidence for rearrangement of hydrogens prior to dissociation of the corresponding molecule ions has been reported by several workers (1, 2, 8). Some migration of deuterium atoms is reported in a recent paper on the mass spectra of deuterated butanes (5). Migration of atoms and isomerization of ionized molecules has been referred to by McDowell (4) in an interpretation of mass spectra based on excited molecular states. Processes of this type are of special interest because of the insight they provide into the nature of bonding forces in molecular ionic states.

The present study of the mass spectrum of 1-butene-4-d_3 arose in connection with mass spectral analysis of the pyrolysis products of this compound and of the light isomer 1-butene.

EXPERIMENTAL

The 1-butene used for purposes of comparison was Research Grade (99.88%) obtained from the Phillips Petroleum Company, Bartlesville, Okla. The deuterated butene was kindly prepared for us by Dr. L. C. Leitch of the National Research Laboratories, Ottawa, according to the following method:

$$CCl_3Br + CH_2=CH—CH_2Cl \xrightarrow{h\nu} CCl_3CH_2—CHBr—CH_2Cl,$$

$$CCl_3CH_2CHBrCH_2Cl \xrightarrow{Zn} CD_3CH_2CH=CH_2.$$

[1]*Manuscript received June 1, 1956.*
Contribution from the Department of Chemistry, The University of British Columbia, Vancouver, B.C.
[2]*This work was done under Defence Research Board Grant 5001-10 Project No. D44-50-01-10.*

The product was shown by analysis to be almost 100% C=C hydrocarbon. A preliminary mass spectrometric analysis using 10 volt electrons gave an uncertain result but indicated that the sample was better than 90% 1-butene-4-d_3. Conclusive proof of the purity of the compound was obtained by analysis with a Varian high resolution nuclear magnetic resonance (NMR) spectrometer. The NMR spectrum of the 1-butene is shown in Fig. 1(*a*). The peaks labelled *a*, *b*, *c*, and *d* are proton resonance absorption peaks for the hydrogens located on the carbons as follows:

$$\underset{a}{CH_2}=\underset{b}{CH}-\underset{c}{CH_2}-\underset{d}{CH_3}$$

The theoretical relative intensities of the two groups of peaks for 1-butene can be expressed as

$$(a+b)/(c+d) = (2+1)/(2+3) = 3/5.$$

The actual ratio found by measuring the area under the peaks was 3/5.8.

Fig. 1(*b*) shows the NMR spectrum of the deuterated butene. The identity

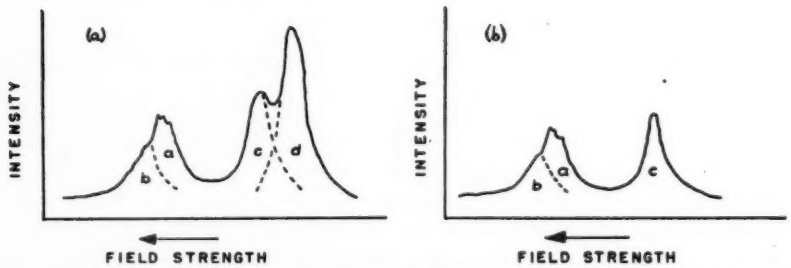

FIG. 1. (*a*) NMR absorption spectrum of $CH_3CH_2CH=CH_2$. (*b*) NMR absorption spectrum of $CD_3CH_2CH=CH_2$.

of the *a* and *b* peaks with those shown in Fig. 1(*a*) is obvious. The *d* peak of the CH_3 group in 1-butene has completely disappeared in the deuterated compound.

Deuterium atoms, having an even number of nucleons, do not exhibit NMR absorption. The relative intensities of the groups in

$$\underset{a}{CH_2}=\underset{b}{CH}-\underset{c}{CH_2}-\underset{d}{CD_3}$$

should be

$$(a+b)/(c+d) = (2+1)/(2+0) = 3/2.$$

The observed ratio was 3/2.26. The complete absence of a '*d*' branch in the spectrum of the deuterated compound was taken as conclusive evidence that the methyl group was completely deuterated, within the sensitivity of detection of the analytical method. The relative intensities of the *a*, *b*, and *c* branches demonstrate the absence of deuterium in the groups to which these peaks correspond.

As a check on the results obtained by NMR a comparison of the infrared

spectra of the two butenes was made using a Perkin-Elmer double beam spectrophotometer. A complete interpretation of the spectra obtained has not yet been achieved but a preliminary band assignment confirms the results obtained by NMR.

The mass spectrum of the light butene is presented in Fig. 2 and that of the deuterated compound in Fig. 3. Fifty-volt electrons were used in obtaining

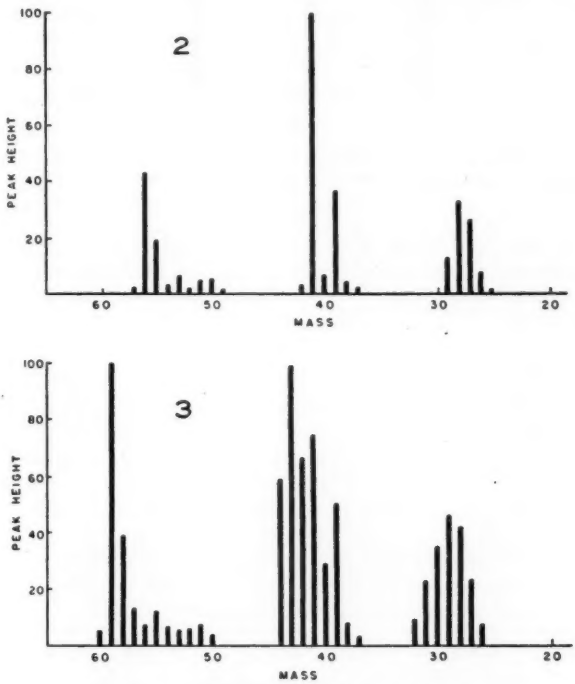

FIG. 2. Mass spectrum of $CH_3CH_2CH{=}CH_2$.
FIG. 3. Mass spectrum of $CD_3CH_2CH{=}CH_2$.

these spectra. The intensity of the largest peak in each spectrum is assigned a value of 100 in the usual way. Normalized spectra for both compounds are presented in Fig. 4. Here the total ion intensities for the C_4, C_3, C_2, and C_1 groups of ions are plotted on a scale such that the C_4 ion intensities are made equal. The solid peaks are for the undeuterated compound.

A detailed study of the fragmentation pattern of the deuterated butene at low electron energies was not made but a few preliminary results showing the intensities of various fragments as a function of electron energy are presented in Table I. The relative intensities at 50 electron volts are also shown.

Results obtained for the pyrolysis of the two butenes provided an interesting basis for comparison of the thermal and electron-impact modes of dissociation. The results given in Table II show the distribution of the principal products

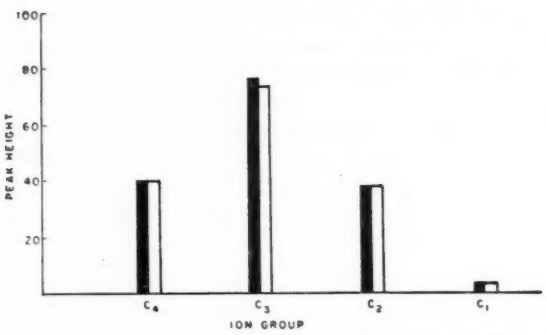

FIG. 4. Normalized spectra of $CH_3CH_2CH{=}CH_2$ (black) and $CD_3CH_2CH{=}CH_2$ (white) showing the relative total intensities for each group of ions.

TABLE I

VARIATION OF C_3 ION INTENSITY WITH ELECTRON ACCELERATING POTENTIAL FOR $CD_3CH_2CHCH_2$

Electron accelerating potential (volts)	Ion intensity (arbitrary units)			
	41	42	43	44
13.0	1.0	3.0	5.0	2.0
15.0	4.0	8.0	14.0	6.0
17.0	12.0	20.5	32.0	16.0
50.0	74.3	67.0	99.3	59.0

TABLE II

PYROLYSIS PRODUCTS FOR THE TWO BUTENES AFTER 5.0 MIN. AT 552°C.

	$CH_3CH_2CHCH_2$ (vol. %)	$CD_3CH_2CHCH_2$ (vol. %)
Methane	24.0	24.0
Ethane	5.3	5.2
Ethylene	8.3	9.0
Propylene	13.0	13.6

for the pyrolysis of 100 mm. of each hydrocarbon in a static system for 5 min. at 552°C. The analyses were performed by gas chromatography, using both adsorption-elution and partition-elution methods.

DISCUSSION

The mass spectrum of the light butene shows clearly that the most abundant fragment produced by electron impact is the $C_3H_5^+$ ion, formed presumably as a consequence of the preferred rupture of the $CH_3{-}CH_2CHCH_2$ bond. This ion would be expected to have the allyl structure, $CH_2CH\dot{C}H_2$, but by rearrangement could assume structures such as $CH_2CH_2\dot{C}H$ or $CH_3CH_2\dot{C}$. A $C_3H_3^+$ fragment is also relatively abundant. The spectrum of the deuterated compound is markedly different from that of the light isotopic molecule. The chief difference is seen in the C_3 group of peaks. The $C_3H_5^+$ ion (mass 41),

which might well be expected to be the most abundant 3-carbon fragment, accounts for only 19% of the total ion intensity. The greater part of the C_3 ion intensity comes from higher masses. Several possible formulas can be written for each of these ions, but the contributions of some of these to the ionic intensities will be negligible. Since the 42 peak from 1-butene is only slightly greater than the C^{13} isotopic peak the contribution of ions equivalent to $C_3H_6^+$ can be neglected. This includes ions such as $C_3H_4D_2^+$ (mass 44) and C_3H_5D (mass 43). In addition since the mass 40 peak from 1-butene is quite small, ions equivalent to $C_3H_4^+$ will make relatively small contributions to the low energy spectrum. Therefore, ions $C_3HD_3^+$ (mass 43), $C_3D_3^+$ (mass 42), and $C_3HD_2^+$ (mass 41) can be neglected. Thus, the greater part of the C_3 ion intensity comes from $C_3H_2D_3^+$ (mass 44), $C_3H_3D_2^+$ (mass 43), $C_3H_4D^+$ (mass 42), and $C_3H_5^+$ (mass 41). It is therefore apparent that migration of the deuterium atoms from the CD_3 group to the rest of the carbon skeleton must have occurred. Rearrangement of hydrogen atoms similar to the rearrangements observed in the deuterated butene will, of course, occur in the light compound but cannot be detected by the present method.

The relative intensities of the ions of masses 41 to 44 (Table I) provide some insight into the relationship between the energy of the ionizing electron and the extent of the migration process. At the lowest electron energy the $C_3H_5^+$ ion makes a comparatively small contribution to the total C_3 ion intensity. The contribution increases markedly with increasing electron energy. This can be seen from Table III in which the variation of the $C_3H_4D^+$ (42)+

TABLE III

VARIATION OF RATIO OF THE SUM OF MASSES 42, 43, AND 44 TO MASS 41 WITH ELECTRON ENERGY

Electron accelerating potential (volts)	$\frac{42+43+44}{41}$
13.0	10.0
15.0	7.0
17.0	5.7
50.0	3.0

$C_3H_3D_2^+$ (43) + $C_3H_2D_3^+$ (44) to $C_3H_5^+$ (41) intensity ratio is presented as a function of electron accelerating potential. It is apparent that deuterium migration is the less probable the higher the energy of the ionizing electron, a consequence presumably of the shorter lifetimes of ions in higher energy states. At lower electron energies the lifetimes of the ions are sufficient, perhaps several vibrations long, to permit extensive rearrangement of the atoms attached to the carbon skeleton.

The relative intensities of the ions of masses 42, 43, and 44 remain approximately constant for all electron energies. This indicates that the migration mechanism does not depend on the energy of the ionizing electron but is the same for all energies once ionization of the molecule has occurred. The factor controlling the extent of migration is the lifetime of the ion, as suggested above.

It can be seen from Fig. 4 that the total intensities of the ions of a given

carbon-number group are the same in the two butenes even though the distribution of intensities and the numbers of fragments observed within the groups are different. This similarity in group intensities shows that deuteration does not have any appreciable effect on the probability of C—C bond rupture. A similar lack of effect in the thermal decomposition of the parent molecule is shown by the distribution of pyrolysis products for the two isotopic compounds given in Table II.

The present work confirms the results reported by Stevenson and Wagner (8) and bears out their prediction that rearrangement of H and D atoms would be more extensive in olefinic than in paraffinic hydrocarbons. This is presumably a consequence of the less localized character of the bonding in the olefinic parent molecule-ion.

The variety of three-carbon fragments formed is evidence of the existence of a number of different modes of decomposition of the ionized molecules. The existence of such modes has been referred to by Rosenstock *et al.* (7) in attempting to calculate the mass spectra of polyatomic molecules from a statistical basis. Migration of deuterium atoms, with the resulting changes in configuration, results in transitions between various close-lying energy levels of the given ionic state. Such transitions are equivalent to the crossing of the corresponding potential energy surfaces. The over-all decomposition pattern of the molecule-ions will depend on the distribution of the ions among the various accessible energy states. Information is not yet available to permit the evaluation of the probabilities of the transitions referred to above. Lennard-Jones and Hall (3) have considered the probability of excitation to various electron states in *n*-octane by calculating the density of positive charge over the octane ion but little is known about the probability of transition between close-lying configurational states in polyatomic molecules.

The extensive migration of isotopic hydrogens observed in the present work casts some doubt on the reliability of the "fragmentation indices" calculated by Magat and Viallard (6) to describe the probability of bond rupture in the dissociation of hydrocarbons by electron impact. The necessity for caution in interpreting the results of mass spectral analyses where deuterium migration can occur is obvious.

ACKNOWLEDGMENT

We are indebted to Drs. C. A. McDowell and D. J. Fabian for helpful discussions, to Dr. C. Reid and Mr. D. A. Cohen for NMR measurements, and to Mr. J. T. Mayhood for infrared analyses.

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STRUCTURE OF A SYNTHETIC POLYXYLOSE[1]

By C. T. Bishop

ABSTRACT

D-Xylose has been condensed under the catalytic action of hydrogen chloride to yield 5.6% polyxylose having a number average degree of polymerization (D.P.) of 10 or greater. The polyxylose was shown to be highly branched with a predominance of the glycosidic bonds in the α-configuration. Estimation and identification of the hydrolysis products of the methylated polyxylose showed that the glycosidic linkages 1→4: 1→2: 1→3 occurred in a frequency ratio of 6.5: 3: 1.

In the presence of an acid catalyst monosaccharides may condense to form reversion products and there are many reports about the preparation and structures of low molecular weight oligosaccharides, mainly disaccharides, thus formed (11, 17, 19, 20, 22). There are a limited number of references to higher molecular weight polysaccharides, having a degree of polymerization (D.P.) greater than 10, formed by reversion. Pacsu and Mora (12) reported the isolation of a polyglucose having a D.P. of 37–42 and claimed that similar products could be obtained from D-mannose, D-fructose, L-arabinose, maltose, and cellobiose. However, no details were given of the polysaccharides formed from these latter sugars. Preparation of these polymers was accomplished by low temperature evaporation of a concentrated solution of the monosaccharide in 5% hydrochloric acid. Kent (8) has synthesized glucose polymers by heating glucose monohydrate with thionyl chloride and Theobald and Twigg (18) also used this method. Ricketts (14, 15) improved on these methods of polysaccharide syntheses by allowing crystalline D-glucose or its monohydrate to deliquesce in the presence of hydrogen chloride. It was postulated that by this process, the molecules of D-glucose, which in the crystalline state are as near to each other as possible, must pass through the optimum distance for bond formation as they dissolve.

The linkages formed in the reversion of hexoses by acid in the experiments just summarized were primarily 1→6 and were predominantly in the α-configuration. Of the glycosidic linkages other than 1→6, the 1→4 was prevalent but there was a notable absence of the 1→3. Since the final composition of a system undergoing acid reversion is determined by equilibria between hydrolytic and condensation reactions, the preferential occurrence of 1→6 over 1→4 over 1→3 linkages could be caused by (*a*) differences in acid-stability of the linkages once formed or (*b*) differences in reactivities of hydroxyl groups. There is evidence in favor of both effects: (*a*) Wolfrom *et al.* (24) showed that for glucose disaccharides the α, 1→4 linkage is hydrolyzed by acid four times as rapidly as the α, 1→6 bond, and Ricketts and Rowe (15) found that maltose is not incorporated as such into a polyglucose on acid reversion but yields a product very similar to that obtained from glucose, with a predominance of

[1]*Manuscript received May 24, 1956.*
Contribution from the Division of Applied Biology, National Research Council, Ottawa, Canada. Issued as N.R.C. No. 4054.

1→6 links. (*b*) It is known that under the conditions of acid reversion, high sugar concentrations, and low temperatures, di- and oligo-saccharides accumulate. The equilibrium hydrolysis⇄condensation must then be shifted towards the right and it would be expected that reactivities of the hydroxyl groups would determine the location of the glycosidic bonds. In this regard it should be noted that the frequency of occurrence of specific glycosidic bonds in reversion products agrees with the differences in reactivities of the hydroxyl groups as determined by other means (16). Therefore, in acid reversion of hexoses, since both viewpoints (*a*) and (*b*) lead to the same result, it appears that the most stable linkages are formed at the most reactive hydroxyl groups. There is little quantitative data on the different glycosidic bonds formed in reversion of sugars, particularly those formed at secondary hydroxyl groups. The problem is difficult in the hexose series where the great preponderance of 1→6 linkages interferes, but the difficulty could be overcome by using a pentose which, in its stable pyranose form, has no primary hydroxyls. This idea led to a study of the polymerization of D-xylose and estimation of the frequency of occurrence of different glycosidic linkages in the polymer by classical methylation techniques as reported here.

D-Xylose was polymerized under the same conditions used by Ricketts (14) for preparing a polyglucose. Extraction of the dried non-dialyzable material from this condensation with different concentrations of ethanol yielded the three fractions listed in Table I. The 5.6% yield of polyxylose having a D.P.

TABLE I

SYNTHETIC XYLANS

Fraction	Yield	$[\alpha]_D^{25}$ (c = 2 in water)	Degree of polymerization
1	1.32 gm. (2.64%)	+93°±1°	7
2	1.11 gm. (2.24%)	+88°±1°	10
3	1.69 gm. (3.38%)	+55°±2°	15

of 10 or greater was low in comparison with that obtained from glucose, 17–45% (14, 15), and was undoubtedly caused by decomposition of D-xylose under the strong acidic conditions. The D.P. values given are number averages, having been determined by hypoiodite oxidation, and hence represent the repeating unit of the polyxylose. The actual particle size may, of course, be much larger. The high positive rotations of the products showed that the glycosidic linkages were predominantly in the α-configuration but the decrease in rotation with increasing D.P. would indicate the presence of some β-linkages. This is in agreement with the results of Thompson *et al.* (19) who found both α- and β-links in reversion products of D-glucose. When oxidized by periodate, Fractions 1, 2, and 3 respectively consumed 1.22, 0.97, and 0.97 moles of oxidant per mole anhydro-D-xylose with the concurrent release of 0.85, 0.50, and 0.40 moles of formic acid per mole anhydro-D-xylose. Fraction 1 was obviously overoxidized but the results for Fractions 2 and 3 were indicative of highly branched polyxyloses containing 3–4 non-reducing terminal xylose units.

Fraction 3 was methylated and hydrolyzed to yield the methyl ethers of D-xylose shown in Table II. These compounds were separated by partition on

TABLE II

COLUMN CHROMATOGRAPHIC SEPARATION OF HYDROLYSIS PRODUCTS OF METHYLATED SYNTHETIC POLYXYLOSE

Receiver number	Component	Chromatographic identity	Yield, mgm. (mM.)	$[\alpha]_D^{25}$ (c = 1% in water)
96–125	1	2,3,4-Tri-*O*-methyl-D-xylose	214 (1.1)	+19°±2°
130–169	2	2,3-Di-*O*-methyl-D-xylose	441 (2.5)	+22°±2°
170–200	3	2,4-Di-*O*-methyl-D-xylose	66 (0.37)	+22°±2°
220–360	4	3-*O*-Methyl-D-xylose	285 (1.7)	+18°±2°
379–564	5	D-Xylose	82 (0.55)	+17°±2°
			1088 mgm. = 94.8% recovery	

Celite columns (9) and were identified by isolation of crystalline products. The quantities of these hydrolysis products were in the following approximate molar relationship: 2,3,4-tri-*O*-methyl-D-xylose (3 moles); 2,3-di-*O*-methyl-D-xylose (7 moles); 2,4-di-*O*-methyl-D-xylose (1 mole); 3-*O*-methyl-D-xylose (5 moles); and D-xylose (1 mole). These results confirmed the branched structure predicted by periodate oxidation, and the total number of moles, 17, being an approximation to the nearest whole number is in good agreement with the number average D.P. of 15 determined by hypoiodite oxidation. If the reversion is regarded as a hydrolysis⇄condensation equilibrium then pyranose ring forms should accumulate in the polymer as the less acid-stable furanoside linkages are hydrolyzed, and in the polyglucose formed by acid reversion no infrared absorption associated with furanoside rings was detected (15). Making the reasonable assumption then that the D-xylose units are in the pyranose form, the methylation results showed the presence of thirteen 1→4 links, six 1→2 links, and two 1→3 links in the polyxylose. This gives a frequency ratio for 1→4 : 1→2 : 1→3 of 6.5:3:1. Whether the most stable linkages are formed at the most reactive hydroxyls in D-xylose as in D-glucose is not known yet but the results given here are in agreement with the greater reactivity of the 2 and 4 positions as compared with 3 in D-xylose as determined by partial methylation (1). An estimate of the stabilities of the linkages will require measurement of the relative rates of hydrolysis of xylose disaccharides having 1→2, 1→3, and 1→4 glycosidic bonds.

EXPERIMENTAL

Chromatographic separations on paper strips were carried out in the following solvent systems (v/v): (A) pyridine: ethyl acetate: water—1:2:2, (B) *n*-butanol: ethanol: water—5:1:4, and (C) *n*-butanol saturated with water. Sugars were detected on the papers by silver nitrate (21) and aniline oxalate (7) spray reagents. Evaporations were done at 40° C. or less, and specific rotations are equilibrium values unless otherwise stated. Melting points are corrected.

Preparation of Polysaccharide

Crystalline D-xylose (50 gm.) was spread in a fine layer in a crystallizing dish and allowed to stand for seven days in a closed desiccator over concentrated hydrochloric acid (50 ml.) to which 10 drops of concentrated sulphuric acid had been added (14). The dark sirupy product was stirred into crushed ice and the acid was neutralized with 10% sodium hydroxide. The neutral solution was dialyzed in a cellophane membrane against running, distilled water for 24 hr. Evaporation of the non-dialyzable mixture to dryness, followed by successive, exhaustive extractions of the residue with 100%, 85%, and 75% aqueous ethanol, yielded Fractions 1, 2, and 3 respectively. Further extraction of the residue with more dilute ethanol (e.g. 65%) removed products contaminated with colored impurities formed during the condensation, so no more fractions were isolated. Ethanol was evaporated from each fraction, and aqueous solutions of the residues were freeze-dried yielding white, fluffy powders. Table I shows the yields, specific rotations, and degrees of polymerization determined by hypoiodite oxidation (6) of the three fractions. When the three fractions were hydrolyzed by *N* hydrochloric acid at 97° C., their specific rotations changed in four hours to a constant value of $+19°\pm1°$, equal to that of D-xylose, and xylose was the only sugar detectable by paper strip chromatography (Solvent A).

Periodate Oxidations

Samples (2.03 mgm., 0.0154 mM.) of each fraction were oxidized by periodate at pH 5.7 and 20° C. using the Warburg respirometer for continuous measurement of formic acid production (13). Amounts of periodate consumed were determined, after formic acid production was constant, by the usual excess arsenite method (4, 5). In 65 hr., production of formic acid reached constant values of 0.85, 0.50, and 0.40 moles per mole anhydro-D-xylose unit for Fractions 1, 2, and 3 respectively. Periodate consumptions by these three fractions at the same time and in the same sequence were 1.22, 0.97, and 0.97 moles per mole anhydro-D-xylose unit.

Methylation

Fraction 3 (8.66 gm.) was suspended in tetrahydrofuran (250 ml.) and solid sodium hydroxide pellets (30 gm.) were added. The mixture was stirred vigorously during the dropwise addition of dimethyl sulphate (40 ml.) over an eight hour period and stirring was continued for a further 18 hr. The mixture was then heated to 70° C. and enough water was added to dissolve the inorganic salts. Tetrahydrofuran was removed by evaporation and the residual aqueous solution was cooled to 0° C. before addition of 10% sulphuric acid to pH 8. Sodium sulphate which precipitated was filtered and washed with chloroform and the aqueous filtrate was extracted four times with an equal volume of fresh chloroform. The combined chloroform extracts were dried over anhydrous sodium sulphate and evaporated to a sirup (6.25 gm., $OCH_3 = 34.6\%$). This product was remethylated as just described but the product was isolated this time by continuous extraction of the aqueous solution (pH 8) for 18 hr. with chloroform. The product (4.80 gm.) was a friable solid having no hydroxyl absorption peak at 3400 $cm.^{-1}$ in its infrared spectrum; $[\alpha]_D^{25} = +65°\pm2°$

(c = 0.8% in chloroform). Analysis: Calc. for $C_8H_{18}O_4[C_7H_{12}O_4]_{13}.C_8H_{18}O_5$ ($32\times OCH_3$): OCH_3, 40.5%. Found: OCH_3, 41.8%.

Hydrolysis of Methylated Xylan

The methylated polysaccharide (4.77 gm.) was dissolved in 5% methanolic hydrogen chloride (200 ml.) and the solution was refluxed till it reached a constant rotation (10 hr.). Methanol was evaporated at 37° C. and N hydrochloric acid (100 ml.) was added to the residue. This mixture was then heated on a boiling water bath for seven hours after which the acid was removed by Dowex-2 ion exchange resin (carbonate form). The neutral solution was evaporated to a sirup (3.6 gm.) which qualitative paper strip chromatography in Solvents B and C showed was a mixture of a tri-*O*-methyl xylose, two di-*O*-methyl xyloses, an *O*-methyl xylose, and xylose. By running authentic samples on the same paper strip these components were chromatographically identified as xylose and its following methyl ethers: 2,3,4-tri-*O*-methyl; 2,3-di-*O*-methyl; 2,4-di-*O*-methyl; and 3-*O*-methyl.

Separation of Hydrolysis Products

A portion (1.1 gm.) of the mixture of components from hydrolysis of the methylated xylan was resolved by partition on a Celite No. 535 column (295 gm., 50×5 cm.) using water-saturated *n*-butanol as the developing solvent (9). The separation was carried out by the elution technique and fractions of 7.5 ml. were collected by an automatic device which changed the receiver every three minutes. Every fifth tube was examined by paper strip chromatography (Solvent B) to give a picture of the distribution of sugars, and it was found that a complete separation of each component had been obtained. The portions of eluate containing the individual sugars were evaporated and the residues were redissolved in water. These solutions were then clarified by filtration and evaporated to sirups which were dried to constant weight at 0.02 mm. over phosphoric anhydride. Table II shows the results of the separation.

Identification of Hydrolysis Products

Component 1 had $[\alpha]_D^{25} = +19°\pm2°$ (c = 1% in water) and was chromatographically identical with 2,3,4-tri-*O*-methyl-D-xylose in Solvent B. The sirup crystallized completely after being kept for two days in a desiccator at room temperature and recrystallization from ether yielded 2,3,4-tri-*O*-methyl-D-xylose, m.p. and mixed m.p. 91–92° C., $[\alpha]_D^{27} = +22°\pm2°$ (c = 2% in water); reported (2): m.p. 87–90° C., $[\alpha]_D^{25} = +20°$ (c = 1.5% in water).

Component 2 was a sirup having the same R_f value as 2,3-di-*O*-methyl-D-xylose in Solvent B and $[\alpha]_D^{25} = +22°\pm2°$ (c = 1% in water). The sugar (50 mgm.) was refluxed for three hours with 1.5 moles of aniline in absolute ethanol (2.0 ml.). The solution was evaporated to a sirup which crystallized after nucleation with the anilide of 2,3-di-*O*-methyl-D-xylose (m.p. 124–125° C.). Recrystallization from ethyl acetate yielded 2,3-di-*O*-methyl-*N*-phenyl-D-xylopyranosylamine, m.p. and mixed m.p. 124–125° C., $[\alpha]_D^{27} = +185°\pm5°$ (c = 0.4% in ethyl acetate; reported (3): m.p. 126° C., $[\alpha]_D^{25} = +180°$ (in ethyl acetate).

Component 3, $[\alpha]_D^{25} = +22° \pm 2°$ ($c = 1\%$ in water), was identical with 2,4-di-*O*-methyl-D-xylose on paper chromatograms (Solvent B) and crystallized spontaneously when an aqueous solution of it was evaporated to dryness. Recrystallized from ethyl acetate, the compound had m.p. 110–111° C., unchanged on admixture with an authentic sample of 2,4-di-*O*-methyl-D-xylose, and $[\alpha]_D^{27} = +22° \pm 2°$ ($c = 1.1\%$ in water); reported (1): m.p. 108° C., $[\alpha]_D^{20} = +22°$ (in water).

Component 4 had $[\alpha]_D^{25} = +18° \pm 2°$ ($c = 1\%$ in water) and ran the same as 3-*O*-methyl-D-xylose on chromatograms (Solvents B and C). The sirup was nucleated with an authentic sample of 3-*O*-methyl-D-xylose after which it crystallized slowly over a two-week period. The product, recrystallized from acetone, had m.p. and mixed m.p. 102–103° C. and $[\alpha]_D^{27} = +18° \pm 1°$ ($c = 3.8\%$ in water); reported (10): m.p. 102–103.5° C., $[\alpha]_D^{22} = +17.2°$ ($c = 2\%$ in water).

Component 5, $[\alpha]_D^{25} = +17° \pm 2$ ($c = 1\%$ in water), was chromatographically identical with D-xylose (Solvents A and B) and the sirup crystallized spontaneously. Recrystallization from glacial acetic acid yielded D-xylose, m.p. and mixed m.p. 145–146° C., $[\alpha]_D^{27} = +18° \pm 1°$ ($c = 3.2\%$ in water); reported (23): m.p. 144–145° C., $[\alpha]_D^{22} = +18.5°$ ($c = 10\%$ in water).

ACKNOWLEDGMENTS

The author wishes to thank Dr. F. Smith, Department of Agricultural Biochemistry, University of Minnesota, St. Paul, Minn., for a gift of 3-*O*-methyl-D-xylose. The technical assistance of D. Torley and W. R. Rowsome is gratefully acknowledged.

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THIAZOLES

II. PREPARATION OF ALKYL-2-NITRAMINOTHIAZOLES[1,2]

By Sidney Kasman[3] and Alfred Taurins

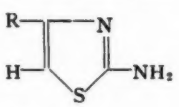
ABSTRACT

1-Chloro-3-methyl-2-butanone and 2-amino-4-*iso*propylthiazole have been synthesized. The mononitration of 2-aminothiazole and five alkyl-2-aminothiazoles in the 2-amino group has been carried out with absolute nitric acid in concentrated sulphuric acid at low temperatures ranging from 0° to −10°. 2-Nitramino- and alkyl-2-nitramino-thiazoles are crystalline, stable compounds. The dinitration of some alkyl-2-aminothiazoles under the same conditions lead to the formation of alkyl-2-nitramino-5-nitrothiazoles. The rearrangement of 2-nitraminothiazole to 2-amino-5-nitrothiazole was studied in the presence of mesitylene for the first time.

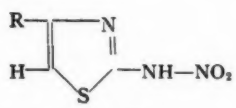
A previous paper (10) of this laboratory described the further nitration of 2-nitramino-5-nitrothiazole with a mixture of 99–100% nitric acid in acetic anhydride. In the same article a summary of previous investigations on the exceptional formation of the dinitration products was given.

The objective of this work was to study the nitration of 2-aminothiazole and several alkyl-2-aminothiazoles under conditions at which the nitration would occur only in the amino group without substituting the hydrogen in the 5-position. The nitrating agent used was absolute nitric acid and the reaction medium was concentrated sulphuric acid. After the completion of this investigation (8) a paper by Dickey, Towne, and Wright (2) appeared dealing partly with the same problem. These authors nitrated 2-aminothiazole in systems containing up to 30% water.

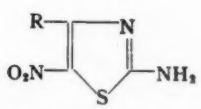
We expected that selective mononitration of the 2-amino group would be favored by the use of a limited quantity of nitric acid, by short reaction time, and by low reaction temperature. The addition of nitric acid to the 2-aminothiazole (I), instead of the reverse, should also foster mononitration through the absence of an excess of nitric acid. It was soon found that one or two excess equivalents of nitric acid were not harmful and increased the yields, that reaction times of the order of a few minutes to an hour were satisfactory, and that the critical factor was the reaction temperature. The working region was found to lie between −10° and 0°.



I: R = H
IV: R = CH_3
VII: R = C_2H_5
X: R = *i*-C_3H_7



II: R = H
V: R = CH_3
VIII: R = C_2H_5
XI: R = *i*-C_3H_7

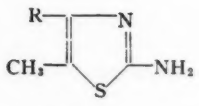


III: R = H
VI: R = CH_3
IX: R = C_2H_5
XII: R = *i*-C_3H_7

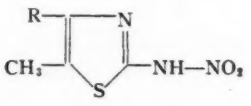
[1]*Manuscript received in original form December 9, 1955, and, as revised, May 23, 1956. Contribution from the Department of Chemistry, McGill University, Montreal, Quebec. The financial support for this work was supplied by the Defence Research Board under D.R.B. Grant No. 9530-06, Project D48-95-30-06.*

[2]*Part I of this series by S. J. Viron and A. Taurins, Can. J. Chem. 31: 885. 1953.*

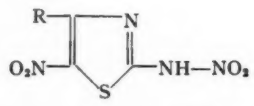
[3]*Holder of a Canadian Industries (1954) Limited Scholarship, 1953–1954.*



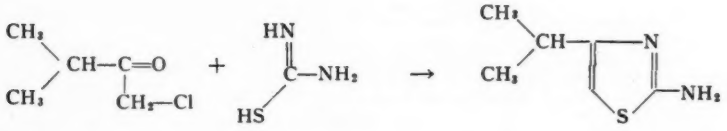
XIII: R = H
XV: R = CH_3



XIV: R = H
XVI: R = CH_3



XVII: R = CH_3
XVIII: R = i-C_3H_7



XIX X

Solutions obtained in this way by the nitration of 2-aminothiazole were invariably found to precipitate a product when poured onto ice. After purification, it was demonstrated to be 2-nitraminothiazole (II) unnitrated in the ring. The 2-nitraminothiazole was found to be a nearly white crystalline solid, acidic to litmus, slightly soluble in water, and quite soluble in dilute sodium hydroxide solution, from which it precipitated on acidification. It gave a positive Franchimont test (5) and deflagrated or exploded when heated to the melting point. The 2-nitraminothiazole was always accompanied by a small amount of 2-amino-5-nitrothiazole (III). This coproduct was precipitated from the acid filtrate by treatment with excess alkali.

The method described for the preparation of 2-nitraminothiazole was found to be applicable to a number of alkyl-substituted thiazoles. At first, 2-amino-4-methylthiazole (IV) (3) was mononitrated to 4-methyl-2-nitraminothiazole (V) in cold sulphuric acid using one equivalent of nitric acid. The reaction was quenched after 15 min. to obtain 56% yield of (V) and 40% of 2-amino-4-methyl-5-nitrothiazole (VI). Lower reaction temperatures favored the formation of the nitramine (V), while higher temperatures favored the formation of the 5-nitro compound (VI).

The next homologous compound, 2-amino-4-ethylthiazole (VII) (9), was nitrated by the same method for 15 min. The unreacted nitric acid was destroyed with absolute alcohol and the reaction was quenched on ice. The yield of 4-ethyl-2-nitraminothiazole (VIII) was 42%, and of 2-amino-4-ethyl-5-nitrothiazole (IX), 4.8%. In another experiment the reaction mixture was stirred for one hour before quenching the reaction. No nitramine could then be isolated, but a 68% yield of (IX) was obtained. These two nitration experiments demonstrated the rearrangement of the nitramine (VIII) into amino–nitro compound (IX), and its importance in the formation of 2-amino-5-nitrothiazoles.

We synthesized for the first time 2-amino-4-*iso*propylthiazole (X) by condensing 1-chloro-3-methyl-2-butanone with thiourea. The 1-chloro-3-methyl-2-butanone (XIX) was prepared in 38% yield by the action of diazomethane on 2-methylpropionyl chloride, followed by treatment with dry hydrogen

chloride. Mononitration of 2-amino-4-*iso*propylthiazole (X) in cold sulphuric acid gave a 37% yield of pure 4-*iso*propyl-2-nitraminothiazole (XI) and a 32% yield of 2-amino-4-*iso*propyl-5-nitrothiazole (XII).

As an example of a 2-amino-5-alkylthiazole, 2-amino-5-methylthiazole (XIII) gave on nitration, at best, a 22% yield of 5-methyl-2-nitraminothiazole (XIV) when the unreacted nitric acid was destroyed with alcohol. The mononitration of 2-amino-4,5-dimethylthiazole (XV) (4, 7) tended to give gummy products, but a small amount of 4,5-dimethyl-2-nitraminothiazole (XVI) was isolated.

Dinitration

The dinitration of two 2-amino-4-alkylthiazoles was carried out in concentrated sulphuric acid at low temperature using 2.2 to 2.4 equivalents of absolute nitric acid. The nitration of 2-amino-4-methylthiazole (IV) gave a 41% yield of pure 4-methyl-2-nitramino-5-nitrothiazole (XVII) and a 34% yield of 2-amino-4-methyl-5-nitrothiazole (VI). Under similar conditions 2-amino-4-*iso*propylthiazole (X) gave 2-nitramino-5-nitro-4-*iso*propylthiazole (XVIII) (45% yield), which was accompanied by a 13% yield of 2-amino-4-*iso*propyl-5-nitrothiazole (XII).

Rates of Nitration

In order to compare qualitatively the rates of nitration of the 2-amino group and hydrogen atom in the 5-position, a sample of 2-aminothiazole was nitrated at −5° and aliquots of the cold reaction mixture were withdrawn 7 and 67 min. after the addition of nitric acid was completed. After removal, these two aliquots were promptly quenched on ice. The precipitated 2-nitraminothiazole (II) was filtered off and crystallized from 95% ethanol. The yields were corrected for solubility in cold 95% ethanol (0.55 gm./100 ml.). The acid filtrates were rendered alkaline and the precipitated 2-amino-5-nitrothiazole (III) was crystallized from 95% ethanol. The results are listed in Table I.

TABLE I

Aliquot	Yield of 2-nitraminothiazole(II)	Yield of 2-amino-5-nitrothiazole (III)
1	1.95 gm.; 37.4%	0.16 gm.; 3.1%
2	1.72 gm.; 33.0%	0.16 gm.; 3.1%
3	None	2.14 gm.; 52.7%

This experiment shows that at −5° the rate of formation of 2-nitraminothiazole is quite high and involves an equilibrium reaction. Under the same conditions the process which forms 2-amino-5-nitrothiazole does not proceed at a significant rate. The small initial yield of 2-amino-5-nitrothiazole must have been formed under conditions peculiar to the beginning of the reaction. Otherwise the yield of (III) would be expected to increase markedly in one hour over the 3% found after only seven minutes, since nuclear nitro groups are introduced in an irreversible reaction. Local heating was unavoidably

produced during the dropwise addition of nitric acid solution to the reaction mixture. It was probably due to the exothermic nature of the nitration reaction and to the heat of dilution of nitric acid in sulphuric acid.

In another nitration, two equivalents of nitric acid were used, and 6.4% of 2-amino-5-nitrothiazole was isolated, supporting the view that transient high temperatures were responsible for the initial formation of this nitration product.

The residual solution, the third aliquot of the first batch, was warmed gently. Its temperature rose suddenly to 140° and then dropped rapidly. In this process all of the 2-nitraminothiazole, as well as some of the hitherto unreacted 2-aminothiazole, appeared in highly augmented yield (52.7%) of 2-amino-5-nitrothiazole. This result indicates the high activation energy and great temperature dependence of the nuclear nitration reaction.

Another pair of nitration experiments was carried out with 2-amino-4-ethylthiazole (VII) at temperature below 0°, with one equivalent of nitric acid. Five minutes after the nitric acid was added, 42% of 4-ethyl-2-nitraminothiazole (VIII) and 4.8% of 2-amino-4-ethyl-5-nitrothiazole (IX) were isolated. After 65 min. at 0°, only (IX) in 68% yield could be isolated. The +Is effect of the 4-ethyl group has undoubtedly activated the 5-position to nitronium ion attack, as compared with the 5-position of 2-aminothiazole. Nevertheless, the rate of nuclear nitration is still very slow compared with the rate of nitration of the 2-amino group. The final isolation of only 2-amino-4-ethyl-5-nitrothiazole is another example of a slow irreversible nuclear nitration reaction prevailing over a fast reversible nitration reaction of the amino group.

Rearrangement Experiments

The rearrangement of 2-nitraminothiazole to 2-amino-5-nitrothiazole when added to concentrated sulphuric acid was observed to proceed readily. The mechanism of the acid-catalyzed rearrangement of aromatic nitramines has not been extensively investigated, and some uncertainty remains in the interpretation of results. Bradfield and Orton (1) measured photometrically the rate of isomerization of 2-bromo-4-methyl-1-nitraminobenzene to 6-amino-2-bromo-4-methylnitrobenzene. Hughes and Jones (6) studied the rearrangement of nitraminobenzene in acidic medium in the presence of a foreign substance which can be easily nitrated. They added 1,4-dimethylbenzene, phenol, or dimethylaniline, which were nitrated by the rearranging nitramine. They found that the compounds mentioned above gave complicated nitration mixtures when used as the foreign substance.

We made a search for a compound which could be easily nitrated to yield only one mononitration product which would be steam-volatile for easy separation and solid for easy purification. We found that 1,3,5-trimethylbenzene (mesitylene) satisfied these criteria. To ensure the formation of only mononitromesitylene, *two* molar equivalents of mesitylene were suspended in stirred concentrated sulphuric acid at 0° and one molar equivalent of 2-nitraminothiazole was added in portions. From the diluted reaction mixture, an oily solid was separated by steam distillation. The solid was filtered from the oil which was reduced with tin and hydrochloric acid and acetylated with

acetic anhydride. When it had been purified, the original solid proved, surprisingly, to be 2,4-dinitro-1,3,5-trimethylbenzene.

Since mesitylene was present in excess during the rearrangement and since a nitro group tends to deactivate an aromatic ring, it is difficult to account for the exclusive formation of dinitromesitylene. If nitromesitylene is much more soluble in sulphuric acid than mesitylene, it is understandable that the homogeneous reagent reacts more quickly than the heterogeneous one.

The nitration of added mesitylene leaves little doubt that in the rearrangement of 2-nitraminothiazole, an intermolecular mechanism is important.

EXPERIMENTAL

2-Nitraminothiazole (*II*)

(*a*) To 30 ml. of concentrated sulphuric acid was added 21.0 gm. (0.21 mole) of 2-aminothiazole (I) in portions, while stirring and cooling. The temperature was kept below 0° by intermittent cooling with a dry ice – alcohol bath. About 15 ml. of concentrated sulphuric acid was cooled to −30° and 9.2 ml. (13.9 gm., 0.22 mole) of absolute nitric acid was added to it. The mixture was stirred as it warmed up and became fluid. The mixed acid solution was added dropwise to the stirred amine sulphate mixture during 15 min. The reaction temperature was maintained at 0±3°. The solution was then stirred for 55 min. at 2–3° and poured onto 65 gm. of chipped ice. The resulting creamy precipitate was filtered off under suction and crystallized immediately from 300 ml. of 95% alcohol. The crystals were in the form of needles. The pure crystalline 2-nitraminothiazole (II) exploded at 204.7°. The yield was 7.2 gm. (23.7%).

A 0.1478 gm. sample of (II) required 10.95 ml. of 0.0926 *N* sodium hydroxide solution for neutralization. Equiv. wt. Calc. for $C_3H_3O_2N_3S$: 145.1. Found: 145.7. Anal. Calc. for $C_3H_3O_2N_3S$: C, 24.82; H, 2.08%. Found: C, 25.11; H, 2.29%.

(*b*) In another preparation, 5.00 gm. (0.05 mole) of (I) in sulphuric acid was nitrated with 4.17 ml. (6.30 gm., 0.10 mole) of nitric acid in sulphuric acid. The mixed acid was added during 55 min. while the reaction temperature was kept below 0°. After the nitric acid was added, stirring and cooling was continued for two min. and then 5 ml. of methanol was run in during eight minutes, while the temperature was kept below 0°. Stirring was continued for another two minutes and the reaction mixture was poured onto 25 gm. of chipped ice. The precipitated nitramine (II) was filtered off, boiled with 120 ml. of water and some active charcoal, and gravity filtered while hot. This yielded 3.21 gm. of pure dried product (44.3%), m.p. 204.7°. Rendered just alkaline with concentrated ammonia, the diluted sulphuric acid filtrate precipitated 0.56 gm. of 2-amino-5-nitrothiazole (III), which after crystallization from alcohol melted at 195°.

4-Methyl-2-nitraminothiazole (*V*)

To a stirred mixture of 11.4 gm. (0.10 mole) 2-amino-4-methylthiazole (IV) in 15 ml. of sulphuric acid cooled to −8° was added 4.35 ml. (6.61 gm., 0.105 mole) of nitric acid in 7 ml. of sulphuric acid during 50 min. The reaction mixture was then stirred five minutes at 5° and poured onto 35 gm. of chipped

ice. The resulting sludgy precipitate was extracted with 150 ml. of boiling 95% alcohol and filtered while hot. The filtrate was reboiled with charcoal and filtered to give a deep red filtrate. The resulting matted needles were filtered off and the filtrate was reboiled and passed through the sludge again. A second crop of needles was obtained on cooling. The filtrate was reduced to 60 ml., cooled in ice, and diluted with 25 ml. of water. A third crop was obtained. The combined nitramine product weighed 8.96 gm. (56.4%) when dry. Crystallized from 10% acetic acid, 4-methyl-2-nitraminothiazole (V) melted at 190° with decomposition. Anal. Calc. for $C_4H_5O_2N_3S$: C, 30.18; H, 3.14%. Found: C, 30.27; H, 3.29%.

The dilute sulphuric acid filtrate yielded 6.32 gm. (39.8%) of 2-amino-4-methyl-5-nitrothiazole (VI). After two crystallizations from 50% alcohol, it melted at 218–219° with decomposition.

4-Ethyl-2-nitraminothiazole (*VIII*)

A solution of 0.83 ml. (1.26 gm.; 0.02 mole) nitric acid in 1 ml. of sulphuric acid was added to a stirred solution of 2.56 gm. of 2-amino-4-ethylthiazole (VII) in 5 ml. of sulphuric acid at −5° during five minutes. The mixture was stirred for five minutes below 0° and then poured onto 18 gm. of chipped ice. The precipitate of nitramine was crystallized from 150 ml. of 7% acetic acid to yield 1.46 gm. (42.1%) of pure 4-ethyl-2-nitraminothiazole (VIII), melting at 190° with decomposition. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.61; H, 3.96%.

The sulphuric acid filtrate was made alkaline with concentrated ammonia. The precipitate was filtered off and dried to obtain 0.27 gm. (4.8%) of 2-amino-4-ethyl-5-nitrothiazole (IX). After two crystallizations from 50% alcohol it melted at 197.5° with decomposition. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.83; H, 3.98%.

2-Methylpropionyl Chloride

A solution of 106 gm. (1.20 moles) of *iso*butyric acid and 161 gm. (1.35 moles) of thionyl chloride was heated under reflux for one hour and then slowly distilled. The product collected between 86° and 92° weighed about 150 gm. and was obviously contaminated with thionyl chloride. The product was refluxed for two hours with 15 gm. (0.12 mole) of benzoic acid and distilled. The procedure was carried out two more times, finally yielding 90.3 gm. (70.5%) of 2-methylpropionyl chloride, boiling at 92–94°.

1-Chloro-3-methyl-2-butanone (*XIX*)

Diazomethane was generated in the usual way from 100 gm. (0.97 mole) of nitrosomethylurea and dried over potassium hydroxide pellets. The solution was cooled with ice and stirred while 2-methylpropionyl chloride was added dropwise. The solution was allowed to stand for one hour at 5°. Dry hydrogen chloride was then bubbled through the solution for one hour and the ether was distilled off. The residual oil was distilled over at about 60 mm. pressure and then fractionally distilled at atmospheric pressure. The fraction boiling at

149–152° weighed 17.48 gm. (38%). Attempts to prepare the oxime were unsuccessful. The pale yellow liquid had a specific gravity of 1.022 gm./cc. at 28° and a refractive index, n_D^{28} 1.4252. M_D Calc., 30.17. Found, 30.18.

2-Amino-4-isopropylthiazole (*X*)

A mixture of 16.25 gm. (0.135 mole) of 1-chloro-3-methyl-2-butanone, 10.7 gm. (0.140 mole) of thiourea, and 11 ml. of 95% alcohol was warmed under reflux on the steam bath. After a few minutes, a vigorous exothermic reaction occurred. Heating was continued for one hour under reflux and then the condenser was removed to permit alcohol to escape. The residue was made alkaline with concentrated ammonia, diluted with water, filtered to remove an insoluble scum, and extracted with three 35-ml. portions of ether. The extracts were dried over anhydrous magnesium sulphate and distilled to remove ether. The residue was distilled under vacuum to give a readily crystallizing pale yellow oil. Yield 14.88 gm. (77.5%), melting at 48–50°. Picrate: m.p. 216–217° decomp. Anal. Calc. for $C_{12}H_{23}O_7N_5S$: C, 38.83; H, 3.53%. Found: C, 38.96; H, 3.83%.

2-Acetamido-4-isopropylthiazole

A mixture of 1.42 gm. (0.01 mole) of 2-amino-4-*iso*propylthiazole and 3 ml. (3.24 gm., 0.03 mole) of acetic anhydride was warmed briefly on the steam bath to obtain a solution. After it had been left for four hours at room temperature, the solution was poured onto 5 gm. of chipped ice and the resulting white granular precipitate was filtered off and dried. It weighed 1.70 gm. (93.5%). One crystallization from 50% alcohol improved the melting point from 143–144° to 145.8–146.5°. Anal. Calc. for $C_8H_{12}ON_2S$: C, 52.16; H, 6.57%. Found: C, 52.37; H, 6.66%.

4-Isopropyl-2-nitraminothiazole (*XI*)

A solution of 1.45 ml. (2.20 gm., 0.035 mole) of nitric acid and 2 ml. of sulphuric acid was added during 14 min. to a stirred mixture of 4.26 gm. (0.03 mole) of 2-amino-4-isopropylthiazole (X) and 5 ml. of sulphuric acid at −25°. Stirring was continued for 10 min. at −20° and then an excess (2 ml.) of absolute alcohol was cautiously added at −15°. The reaction mixture was rinsed onto 30 gm. of supercooled, chipped ice and the resulting precipitate was filtered off and rinsed with alcohol. It was crystallized from 140 ml. of 50% alcohol to obtain 2.10 gm. (37%) of (XI) in the form of golden needles, melting at 185° with decomposition. Equiv. wt. Calc. for $C_6H_9O_2N_3S$: 187. Found: 184. Anal. Calc. for $C_6H_9O_2N_3S$: C, 38.50; H, 4.85%. Found: C, 38.22; H, 5.07%.

2-Amino-4-isopropyl-5-nitrothiazole (*XII*)

The dilute sulphuric acid filtrate was made alkaline with an excess of concentrated ammonia and the resulting precipitate of (XII) was filtered off and dried. Crude yield: 1.82 gm. (32.4%). After three crystallizations from 50% alcohol, a pure compound, melting at 230–231° with decomposition, was obtained. Anal. Calc. for $C_6H_9O_2N_3S$: C, 38.50; H, 4.85%. Found: C, 38.70; H, 4.80%.

4-Isopropyl-2-nitramino-5-nitrothiazole (*XVIII*)

A solution of 4.00 ml. (6.04 gm., 0.096 mole) nitric acid in 3 ml. of sulphuric acid was added during seven minutes to a stirred mixture of 5.68 gm. (0.04 mole) 2-amino-4-*iso*propylthiazole (X) in 7 ml. sulphuric acid at −17°. The red solution was stirred for 1.2 hr. while immersed in an ice-water bath, which was then removed. The reaction temperature rose to 30° and was reduced by ice cooling. The mixture was then stirred for 4.7 hr. without cooling. An excess of absolute alcohol was added cautiously and the reaction mixture was poured onto 40 gm. of chipped ice. A gummy substance resulted, which was removed and boiled with 300 ml. water. The hot mixture was filtered and the filtrate was cooled. A yellow crystalline precipitate formed and was filtered off. The filtrate was reboiled with the residue to obtain a second crop of crystalline product. The combined yield was 4.17 gm. (45.0%). One crystallization from 220 ml. of 10% acetic and one crystallization from 300 ml. of 1.2 *N* hydrochloric acid gave product (XVIII), which melted with decomposition at 144°. Equiv. wt. Calc. for $C_6H_8O_4N_4S$: 232.2. Found: 231.2. Anal. Calc. for $C_6H_8O_4N_4S$: C, 31.03; H, 3.47%. Found: C, 31.15; H, 3.52%.

5-Methyl-2-nitraminothiazole (*XIV*)

To a stirred solution consisting of 4.56 gm. (0.04 mole) of 2-amino-5-methylthiazole (XIII) in 8 ml. of concentrated sulphuric acid cooled below −15°, was added a solution of 1.98 ml. (3.00 gm., 0.0475 mole) nitric acid in 2 ml. sulphuric acid during 10 min. The resulting solution was stirred and maintained below −10°, while 2 ml. of absolute alcohol was cautiously added to destroy unreacted nitric acid. The solution was quickly rinsed onto 30 gm. of chipped ice. The yellow precipitate that formed was filtered off, rinsed free of acids with water, and vacuum dried. The yield of the product melting at 195–196° with decomposition was 1.39 gm. (21.8%). One crystallization from 5% acetic acid improved the melting point to 198–199° with decomposition. The compound (XIV) could be induced to explode at 202° when heated rapidly. Anal. Calc. for $C_4H_5O_2N_3S$: C, 30.18; H, 3.14%. Found: C, 30.35; H, 3.24%.

4,5-Dimethyl-2-nitraminothiazole (*XVI*)

A solution of 2.56 gm. (0.02 mole) of 2-amino-4,5-dimethylthiazole (XV) in 4 ml. of sulphuric acid was cooled below −5°. Nitric acid (0.92 ml., 1.39 gm., 0.032 mole) dissolved in 1 ml. of sulphuric acid was added dropwise to the above solution with stirring during 10 min. About 0.5 ml. of absolute alcohol was then added cautiously to destroy unreacted nitric acid and the reaction mixture was rinsed onto 10 gm. of chipped ice. The precipitate that formed after a few minutes was rinsed with water and crystallized from 15% acetic acid. On cooling, a small granular precipitate of nitramine formed. The compound (XIV) exploded on heating at 192°. Anal. Calc. for $C_5H_7O_2N_3S$: C, 34.69; H, 4.08%. Found: C, 34.85; H, 4.08%.

Study of the Mechanism of Nitration of 2-Aminothiazole

To a mixture of 10.0 gm. (0.10 mole) of 2-aminothiazole and 15 ml. of sulphuric acid was added 4.35 ml. (6.16 gm., 0.105 mole) of nitric acid in 5 ml. of

sulphuric acid during 10 min. with stirring and cooling to keep the temperature at −5°. After seven minutes, 10 ml. of the solution was pipetted into 10 gm. of chipped ice. The precipitated nitramine was filtered off and crystallized from 70 ml. of 95% alcohol. The purified product weighed 1.57 gm. A saturated solution of 2-nitraminothiazole was found to contain 0.55 gm. of nitramine per 100 ml. of solution. The product must then have contained 0.55 gm. × 0.70 = 0.38 gm. more nitramine before crystallization. Corrected yield 1.57 gm. +0.38 gm. = 1.95 gm. The aliquot was about 0.36 of the total reaction mixture, so when the aliquot was withdrawn there must have been 1.95 gm. ÷ 0.36 = 5.42 gm. of nitramine present, i.e. 37.4% of the thiazole present. Neutralization of the sulphuric acid filtrate gave crude 2-amino-5-nitrothiazole which after one crystallization from alcohol weighed 0.16 gm. dry (3.1%). Similarly, a second aliquot removed 67 min. after the nitric acid was added gave 1.72 gm. (33.0%) of nitramine and 0.16 gm. (3.1%) of 2-amino-5-nitrothiazole. The residual reaction mixture, 0.28 (1 − 0.36 × 2 = 0.28) of the whole, was then warmed gently on the steam bath. The temperature rose suddenly to 140° and the mixture became quite dark. It was warmed an additional 30 min. and then quenched by pouring onto 10 gm. of chipped ice. No nitramine precipitated. On neutralization with ammonia, a precipitate of 2-amino-5-nitrothiazole formed that weighed 2.14 gm. (52.7%) after one crystallization from alcohol. Corrections for solubility were not made to the weights of 2-amino-5-nitrothiazole.

Rearrangement of 2-Nitraminothiazole

To 4.7 ml. of concentrated sulphuric acid, cooled to 0°, was added 2.76 gm. (0.019 mole) of 2-nitraminothiazole, in portions. Local heating could not be avoided as the nitramine came in contact with the acid. After 10 min., the solution was poured onto 8 gm. of ice. A small precipitate (0.10 gm. dry) formed. It was filtered off and the filtrate was made alkaline with concentrated ammonia. The precipitate of 2-amino-5-nitrothiazole weighed 1.37 gm. dry (49.5%) and was pure after one crystallization from 30 ml. 10% acetic acid.

Rearrangement of 2-Nitraminothiazole in the Presence of Mesitylene

Mesitylene (3.31 gm., 0.276 mole) was suspended in 10 ml. of concentrated sulphuric acid by agitation and the mixture was kept near −5°. During 20 min., 2.0 gm. (0.138 mole) of 2-nitraminothiazole (II) was added in small portions. The mixture was then surrounded with an ice-water bath and stirred for 10 hr. The reaction mixture was then diluted to 100 ml. with water and steam distilled until 300 ml. of distillate containing a yellow solid had collected. The distillate was extracted with three 50-ml. portions of ether and the extract was dried (over anhydrous magnesium sulphate) and evaporated. An oily crystalline solid remained. The crystals were filtered from the oil and weighed 0.20 gm. Sublimation at 100° and 1 mm. pressure gave 0.10 gm. of a pale yellow solid melting at 77–83°. Crystallized from 95% alcohol the product melted at 85.0–85.5°. Reported for 2,4-dinitro-1,3,5-trimethylbenzene: m.p. 84°. The oil that was obtained was warmed on the steam bath for several hours with excess of powdered tin and hydrochloric acid. The solution was filtered

from the tin, made alkaline with excess of sodium hydroxide, and filtered from the white precipitate. The precipitate and filtrate were separately extracted with ether and the combined extracts were evaporated nearly dry. The residue was treated with acetic anhydride. Immediately, a precipitate of fine needles formed; m.p. 330–334° decomp. Sublimation at 190° and 0.2 mm. pressure did not improve the melting point. One crystallization from absolute alcohol raised the melting point to 344–346° with decomposition. Reported for 1,3-diacetamido-1,3,5-trimethylbenzene: m.p. 320–325°. Anal. Calc. for $C_{13}H_{18}O_2N_2$: C, 66.64; H, 7.74%. Found: C, 66.48; H, 7.87%.

ACKNOWLEDGMENT

We wish to thank the Canadian Industries (1954) Limited for the scholarship awarded to one of us (S.K.) in 1953–1954. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

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THE REACTIONS OF ACTIVE NITROGEN WITH ORGANIC MOLECULES[1]

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ABSTRACT

The main features of the reactions of active nitrogen with various organic molecules are reviewed, and a unified mechanism outlined to account for at least the more significant experimental observations.

INTRODUCTION

Lewis (23) discovered active nitrogen in 1900. He observed that when nitrogen at low pressure was subjected to a condensed discharge, a yellow mist filled the discharge tube and diffused into the connecting tubes. On breaking the current, a yellow afterglow persisted for several seconds. He showed that the afterglow gave a banded spectrum which could be identified with part of the N_2 spectrum.

In 1911, Strutt (later, Lord Rayleigh) began an extensive study of the physical and chemical properties of nitrogen treated by the Lewis method (12, 13, 34, 40 to 47). He found it to be very reactive chemically. Vapors of many metallic and non-metallic elements (e.g. cadmium, sodium, arsenic, sulphur) were converted to nitrides. Carbon disulphide, sulphur chloride, and hydrogen sulphide yielded a polymeric nitrogen sulphide. Hydrocarbons gave hydrogen cyanide as the main product, while halogenated hydrocarbons gave products from which cyanates were obtained by treatment with potassium hydroxide. All the reactions with organic compounds were accompanied by the brilliant emission of the CN spectrum. The hydrocarbons gave both the red and violet CN bands and the flames appeared lilac in color. When halogen atoms were present in the molecule, the red bands were more strongly developed; this was particularly marked with CCl_4, $CHCl_3$, $CHBr_3$, ethylene dichloride, and ethylidene chloride all of which gave strong orange cyanogen emission. Ethyl chloride and methyl bromide gave flames of intermediate character.

Although most of the early studies of the chemical reactivity of active nitrogen were qualitative in nature (22, 53, 54) the reactions with hydrogen (6, 22, 39) and with nitric oxide and nitrogen dioxide (37) were studied in some detail. Reasonable mechanisms involving atomic nitrogen were suggested for these reactions.

Investigations into the reactions of active nitrogen with various types of molecules, particularly the hydrocarbons and chlorinated hydrocarbons, have been in progress in this laboratory during the past ten years. It seems appropriate at this time to review the main characteristics of these reactions

[1]*Manuscript received March 28, 1956.*
Contribution from the Physical Chemistry Laboratory, McGill University, with financial assistance from the National Research Council.
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and to attempt a consistent interpretation of the reaction mechanisms. In so doing, atomic nitrogen will be assumed to be the main reactive species in active nitrogen, for reasons outlined previously (8).

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The reactions to be discussed were studied in a conventional fast flow system. Nitrogen at a known flow rate was activated by a condensed discharge and introduced into a reaction vessel where it was mixed with the second reactant which also entered at a measured rate through a fine jet. The products were suitably trapped and analyzed by appropriate methods. Experimental details may be obtained by reference to the original papers.

Unsaturated Hydrocarbons

Ethylene

In the first study (18) the products of this reaction were identified as hydrogen cyanide and some ethane. A viscous polymer was also formed, which was probably a polymer of hydrogen cyanide. The yield of hydrogen cyanide increased linearly with ethylene flow rate until a maximum was reached, and then remained constant. Wrede gauge (55) measurements of nitrogen atom concentrations corresponded approximately to the maximum yield of hydrogen cyanide. This indicated that the reaction was fast enough to go to virtual completion in the flow time through the reaction vessel. The yield of ethane increased markedly at higher ethylene flow rates.

In a more detailed study (49) of the reaction, with improved experimental techniques, polymerization of hydrogen cyanide was avoided and material balances of about 98% obtained. It was confirmed that the reaction proceeds by complete consumption of nitrogen atoms in the presence of excess ethylene, and by complete consumption of ethylene in the presence of excess nitrogen atoms. In addition to hydrogen cyanide and ethane, smaller amounts of acetylene, cyanogen, and methane were found in the products. The amount of cyanogen formed increased rapidly with increasing ethylene flow rate when nitrogen atoms were in excess, and then decreased as the ethylene flow rate increased beyond the equivalence point. The amounts of methane and acetylene showed similar behavior, although the change in yield was less striking. At the flow rate where both ethylene and nitrogen atoms were completely consumed, the products of the reaction were hydrogen cyanide (75%), ethane (10%), methane (9%), acetylene (3%), and cyanogen (2%).

Acetylene

The products of this reaction were (50) hydrogen cyanide, a polymer that contained approximately 32% nitrogen, and smaller amounts of cyanogen, methane, and hydrogen. At very low flow rates of acetylene, corresponding to at least a sevenfold excess of nitrogen atoms, the only product was polymer. The yield of hydrogen cyanide and polymer increased to constant values with increase of acetylene flow rate. The yield of cyanogen passed through a maximum at an acetylene flow rate near the value corresponding to the complete consumption of nitrogen atoms. The individual yields of hydrogen

and methane were erratic but the total hydrogen contained in both these products showed a regular dependence on acetylene flow rate, with a maximum yield for a flow rate slightly greater than that required for complete consumption of nitrogen atoms.

Propylene

Hydrogen cyanide and ethylene were the main products of this reaction (48), together with smaller quantities of ethane and propane, and traces of acetylene and of a C_4 fraction. The appearance of C_2 hydrocarbons as the principal product leaves little doubt that the main reaction is the removal of one carbon atom by an attacking nitrogen atom. The yields of propane and ethane paralleled the amounts of propylene and ethylene recovered, and it may be concluded that the saturated products were formed mainly by hydrogenation of the corresponding olefin.

Butenes

The reactions of nitrogen atoms with butene-1, *cis*-butene-2, and isobutene (16) all gave hydrogen cyanide as a main product, together with propylene and ethylene, and smaller quantities of butane, propane, ethane, and methane. All the reactions showed complete consumption of nitrogen atoms at high hydrocarbon flow rates. Apparently the first step in all three reactions led to the formation of hydrogen cyanide, propylene, and a hydrogen atom. The order of reactivities with nitrogen atoms was butene-1 > *cis*-butene-2 > isobutene. Increasing temperature favored the reactions of butene-1 and *cis*-butene-2, but not that of isobutene, so that the lower rate of the isobutene reaction is probably the result of a lower steric factor.

Saturated Hydrocarbons

Methane

Hydrogen cyanide is the only product that has been detected in this reaction (3, 15) in the type of system used. Hydrogen cyanide production was small at all flow rates at temperatures below about 250°C. At higher temperatures, the yield of hydrogen cyanide was low at low methane flow rates but increased rapidly as the methane flow rate was increased. This effect appeared to be due to attack on methane by hydrogen atoms, since the initial low rates of HCN formation could be markedly increased by the addition of appropriate amounts of atomic hydrogen to the system.

Ethane

The only product detected in this reaction was hydrogen cyanide (3, 15), and a good carbon balance was obtained. At temperatures above 165°C., the reaction was found to proceed by complete consumption of nitrogen atoms when ethane was in excess. Under these conditions, production of hydrogen cyanide corresponded to about 85% of the atom concentration inferred from Wrede gauge measurements. When the reaction was studied over a wide range of temperature (15), there appeared to be a distinct difference in activation energies at low and high temperatures.

Propane

The products of this reaction were identified (31) as hydrogen cyanide, acetylene, ethylene, and ethane. Complete consumption of nitrogen atoms was not attained at 63°C., but was attained at 250°C. for a ratio of propane to nitrogen atoms greater than 1.3. Of particular significance was the recovery of ethylene and acetylene in the region of incomplete consumption of nitrogen atoms. The reaction of N atoms with these unsaturated compounds is at least 10 times more rapid than the reaction with propane, so that the recovered ethylene and acetylene can represent only a small fraction of the amounts formed.

Butanes

Hydrogen cyanide and smaller amounts of ethylene and acetylene were obtained from both *n*-butane and isobutane (2). The predominance of unsaturated hydrocarbons in the secondary products was similar to that found for propane, and the amounts formed in the course of reaction must have been much greater than the amounts recovered.

Neopentane

Large quantities of hydrogen cyanide and small quantities of ethylene, acetylene, propylene, and propane were obtained from this reaction (32). Complete consumption of active nitrogen was attained only at 250°C. for a ratio of neopentane to nitrogen atom flow rates greater than 1.3. As with ethane, there appeared to be two activation energies associated with the reaction when it was studied over a wide range of temperature.

Cycloparaffins

The reactions of active nitrogen with cyclopropane and with cyclobutane (25, 30) are similar to the reactions with propane and the butanes. Cyclopropane is somewhat less reactive than propane, while cyclobutane and the open chain butanes have comparable reactivities.

Kinetic Data for the Hydrocarbon Reactions

It has not been possible to obtain any values of the activation energies and steric factors for the reactions of active nitrogen with the olefins and acetylene, owing to their relatively high rates. An early attempt (19) to apply diffusion flame technique to the ethylene reaction indicated that the activation energy was probably less than 3 kcal. and the steric factor possibly of the order 10^{-2}.

Orders of magnitude for the activation energies and steric factors of the reactions with saturated hydrocarbons have been estimated from rough values of the second order rate constants calculated for hydrogen cyanide production at different temperatures. The calculations have generally been made assuming both streamlined and turbulent gas flow through the reaction vessel. The activation energies and steric factors that have been obtained are given in Table I.

TABLE I

Hydrocarbon	E (kcal.)		P		Ref.
	Streamlined flow	Turbulent flow	Streamlined flow	Turbulent flow	
Methane*	11 to 13		10^{-3} to 10^{-2}		(3, 15)
Ethane	6.2	7.9	3×10^{-3}	7×10^{-2}	(3)
High temp. range	5.7	6.3	6.4×10^{-4}	2.0×10^{-3}	(15)
Low temp. range	2.7	2.4	1.4×10^{-5}	1.2×10^{-5}	
Propane	5.1	6.2	9.1×10^{-4}	2.1×10^{-3}	(31)
n-Butane	3.6		4.5×10^{-4}		(2)
Isobutane	3.1		4.4×10^{-4}		(2)
Neopentane					
High temp. range	6.5	7.7	2.7×10^{-4}	4.9×10^{-3}	(32)
Low temp. range	2.0	2.0	1.1×10^{-6}	3.3×10^{-5}	
Cyclopropane	3.2	4.0	1.9×10^{-5}	5×10^{-4}	(25, 30)
Cyclobutane	4.6	6.4	1.5×10^{-4}	4.1×10^{-3}	(30)

**Values for this reaction might have little or no significance owing to demonstrated complications by hydrogen atom reactions. For the same reason, no attempt is made to discuss this reaction in the present paper.*

Alkyl Chlorides

In their rates, these reactions appeared to resemble the analogous reactions with unsaturated hydrocarbons (7). The reactions of all the halides yielded hydrogen cyanide and hydrogen chloride as main products, and small amounts of cyanogen and a polymer that contained carbon, hydrogen, nitrogen, and chlorine. No cyanogen chloride, chlorine, or methane was obtained from any of the reactions. The halides, other than methyl chloride, yielded small amounts of C_2 hydrocarbons (mainly ethylene and acetylene) while the propyl chlorides also gave small yields of C_3 hydrocarbons (mainly propylene). At higher flow rates of the organic chlorides, the yields of products approached limiting values. With methyl chloride, an increase in limiting yield with increase of temperature was observed. It was also observed with methyl chloride that some unchanged reactant was recovered at lower flow rates, in spite of a linear relation between product formation and methyl chloride flow rate.

Methyl Cyanide

The main product of this reaction, over a wide temperature range, was hydrogen cyanide (11). Smaller amounts of cyanogen, methane, ethane, ethylene, acetylene, and (probably) methyl isonitrile were also recovered. The yields of primary products, in relation to the methyl cyanide flow rate, indicated complete consumption of active nitrogen at each temperature, but the maximum yield increased markedly with increase of temperature (cf. methyl chloride).

Methylamine

This reaction yielded hydrogen cyanide and smaller amounts of ammonia and a polymer, together with traces of cyanogen, methane, ethane, ethylene, and acetylene (14). The rates of methylamine destruction and hydrogen cyanide formation increased, and polymer formation decreased, with increase of temperature.

REACTION MECHANISMS

On the basis that atomic nitrogen is responsible for the reactions of active nitrogen with organic molecules (8), it is possible to calculate the energetics of individual reaction steps and, with due regard for the uncertainty in many of the energy values used, to suggest energetically reasonable mechanisms to explain the experimental results.

The products of the atomic nitrogen reactions with saturated hydrocarbons of more than two carbon atoms are generally similar to those of the reactions with the corresponding olefins. This similarity is strongly emphasized by the behavior of the alkyl halides in their resemblance to the olefins when attacked by nitrogen atoms (7). It seems reasonable, therefore, to suggest similar mechanisms for molecules with the same number of carbon atoms. It is convenient to discuss first the probable mechanisms for reactions of the olefins, as a basis for a unified mechanism for the other reactions.

Olefins

Ethylene

The only reaction with ethylene that is energetically favorable is

$$N + C_2H_4 \rightarrow HCN + CH_3 + 62 \text{ kcal.}^3 \qquad [1]$$

This reaction involves both a change in spin (8) and the movement of a hydrogen atom from one carbon atom to the other. There is every reason to expect that a nitrogen atom and an ethylene molecule will form a relatively long-lived complex even before the change in spin occurs.[4] The emission of the reaction flame and the formation of cyanogen and acetylene provide direct evidence that such complexes are formed (see below). Thus, it seems quite possible that the complex will have sufficiently long lifetime to permit both the change in spin and the movement of the hydrogen atom (which might take place after the change in spin).

The observed products from ethylene, together with the results obtained in a study of the reaction of azomethane with nitrogen atoms (1), indicate that methyl radicals formed in reaction [1] react very rapidly with nitrogen atoms,

$$N + CH_3 \rightarrow HCN + 2H + 10 \text{ kcal.} \qquad [2]$$

Reaction [2] is spin-allowed for three-eighths of the collisions (8) and should not have a significant energy barrier. Most of the hydrogen atoms formed by

[3] *Values for the heats of reaction have been calculated from heats of formation given in the Appendix.*

[4] *The repulsion due to exchange forces during the initial approach of the nitrogen atom should be small since p-electrons are involved, and delocalized orbitals embracing the π-orbitals of the carbon–carbon bond and the nitrogen atomic orbitals should lead to considerable lowering of the potential energy, particularly after the change in spin has occurred (8).*

reaction [2] must ultimately have recombined to form H_2, although this was not determined directly. However, the manner in which ethane production varied with ethylene flow rate (49) at the higher flow rates where olefin was in excess shows that most of the ethane in this region was probably formed by the well-known reactions

$$H + C_2H_4 \rightarrow C_2H_5, \quad [3]$$

$$C_2H_5 + H_2 \rightarrow C_2H_6 + H. \quad [4]$$

Hence, reaction [2] must form predominantly two hydrogen atoms rather than molecular hydrogen.

The sharp maximum in the cyanogen production from ethylene makes it seem very likely that cyanogen was formed by reaction between a nitrogen atom and a nitrogen atom – ethylene complex. It is possible that some cyanogen might be formed directly,

$$N + N.C_2H_4 \rightarrow 2(CN)_2 + 2H_2 + (91-q) \text{ kcal.}, \quad [5]$$

where q is the heat evolved in forming the complex,

$$N + C_2H_4 \rightarrow N.C_2H_4 + q.$$

However, this reaction involves a great deal of rearrangement, and it appears more likely that cyanogen was formed by recombination of cyanogen radicals. The reaction

$$N + N.C_2H_4 \rightarrow N_2 + C_2H_4 + (226-q) \text{ kcal.} \quad [6]$$

is very exothermic, and there should be a good chance that the C_2H_4 part of the complex receives enough energy to dissociate into very reactive fragments that then react with a nitrogen atom to form CN radicals, e.g.

$$N + N.C_2H_4 \rightarrow N_2 + 2CH_2^* + (68-q) \text{ kcal.}, \quad [7]$$

$$CH_2^* + N \rightarrow CN + H_2 + 104 \text{ kcal.}, \quad [8]$$

$$2CN \rightarrow (CN)_2, \quad [9]$$

where CH_2^* represents a methylene radical in the triplet state.

Cyanogen radicals may also be formed to some extent from simple reactions, e.g.

$$N + CH_3 \rightarrow CN + H + H_2 - 1 \text{ kcal.} \quad [10]$$

However, the predominance of HCN over $(CN)_2$ observed in the products indicates that reaction [10] occurs far less than reaction [2], and the manner in which cyanogen production varies with ethylene flow rate indicates that reactions resulting from recombination of nitrogen atoms are the more important source of CN radicals.

Reaction [8] is sufficiently exothermic to give the electronically excited CN radicals that emit the reaction flame, and the chemiluminescent reaction of nitrogen atoms with methylene radicals (or with CH radicals which can also be formed in exothermic reactions similar to reaction [7]) may well contribute to the reaction flame.

Two of the products, cyanogen (40) and hydrogen cyanide (5), give cyanogen flames with active nitrogen, probably by such reactions as

$$N + N.C_2N_2 \rightarrow N_2 + CN + CN^* + (112-E) \text{ kcal.}, \quad [11]$$

$$N + N.HCN \rightarrow N_2 + CN^* + H + (111-E) \text{ kcal.}, \quad [12]$$

where E is the electronic excitation energy of CN* above the ground state. However, for organic molecules the flame color varies with the reactant, and there seems to be little doubt that there is more than one mechanism of flame emission.[5]

The reactions

$$N + N.C_2H_4 \rightarrow N_2 + C_2H_4^*, \quad [13]$$

$$C_2H_4^* \rightarrow C_2H_2^* + H_2, \quad [14]$$

$$C_2H_2^* \rightarrow C_2H_2, \quad [15]$$

where $C_2H_4^*$ and $C_2H_2^*$ and represent ethylene and acetylene in triplet states, should occur with quite high probability (8), and may well account for the formation of acetylene in the ethylene reaction. The fact that acetylene production decreases more slowly than cyanogen production at the higher ethylene flow rates gives some indication that vibrationally excited molecules may also give some acetylene by the reaction

$$N_2\dagger + C_2H_4 \rightarrow N_2 + C_2H_4^* \quad [16]$$

followed by reactions [14] and [15]. The close analogy between reactions [13] and [16] will be obvious.

These considerations indicate that acetylene and cyanogen are mainly formed as by-products of the recombination of nitrogen atoms. Further evidence for a catalyzed recombination of nitrogen atoms is to be found in the recovery of significant amounts of methane and ethane in the region where ethylene is completely consumed. If the concentration of nitrogen atoms were not reduced markedly in this region by catalyzed recombination, and remained as high as indicated by the maximum hydrogen cyanide recovery, it is difficult to see how reactions which are probably responsible for the formation of methane and ethane in this region, viz.

$$CH_3 + H_2 \rightarrow CH_4 + H, \quad [17]$$

$$CH_3 + H \rightarrow CH_4, \quad [18]$$

$$CH_3 + CH_3 \rightarrow C_2H_6, \quad [19]$$

could compete successfully with the very fast reaction

$$CH_3 + N \rightarrow HCN + 2H. \quad [2]$$

Propylene

The observed production of ethylene in this reaction leaves little doubt that it is a primary product. At first sight, the spin-disallowed reaction

$$N + C_3H_6 \rightarrow HCN + H + C_2H_4 + 27 \text{ kcal.} \quad [20]$$

seems to be the most likely. However, unless there is a great deal of rearrangement remote from the point of attack, nitrogen atom attack at the double bond should lead to ethylidene radicals rather than ethylene. On the other hand, the reaction similar to the main ethylene reaction

$$N + C_3H_6 \rightarrow HCN + C_2H_5 + 65 \text{ kcal.} \quad [21]$$

[5] *Flame emission may also be due in part to resonance transfer from* vibrationally *excited, ground state molecules of nitrogen in active nitrogen (8),*

$$CN + N_2\dagger \rightarrow CN^* + N_2.$$

Since $N_2\dagger$ molecules also lose vibrational energy by collision, predominantly by one-quantum transfers (8), their energy content and hence the energy received by CN radicals may well depend markedly on the presence of foreign molecules.*

might form ethyl radicals with enough energy to permit the reaction

$$C_2H_5 \rightarrow C_2H_4 + H - 38 \text{ kcal.} \quad [22]$$

Reaction [22] has an activation energy of about 40 kcal. (38), so that it would be expected to occur if less than about 20 kcal. involved in reaction [21] resided as translational energy and vibrational excitation of the hydrogen cyanide. Since it certainly requires more than 7 kcal. to form the ethylidene radical from ethylene, it seems likely that the reactions of ethylene and propylene with nitrogen atoms are similar, with the difference that the ethyl radical from propylene decomposes either during or immediately after the primary reaction.

Ethylene formed by reaction [22] would react with nitrogen atoms as outlined previously.

The manner in which production of propane and ethane varied with propylene flow rate immediately suggests that the saturated products were formed by reactions of hydrogen atoms with the corresponding olefins.

Butenes

The reactions of the butenes are very similar to the reaction of propylene and comment is required only for the reaction

$$N + CH_3—CH=CH—CH_3 \rightarrow C_3H_6 + HCN + H. \quad [23]$$

Since movement of a hydrogen atom from one carbon atom to another apparently occurs in the ethylene reaction, and probably also in the propylene reaction, it may seem strange that, for reaction [23], a methyl group should move instead. However, if, as seems likely, the favored line of approach of the nitrogen atom to the double bond is between the two hydrogen atoms of *cis*-butene-2, the closer approach of the nitrogen atom to one of the carbon atoms may prevent the hydrogen atom on this carbon from shifting and the shift of the methyl group should be highly favored energetically. Hence, the reaction probably occurs by

$$N + CH_3—CH=CH—CH_3 \rightarrow CH_3—CH—CH_3 + HCN \quad [24]$$

followed immediately by

$$CH_3—CH—CH_3 \rightarrow CH_3CH=CH_2 + H. \quad [25]$$

Unified Mechanism

On the basis of the previous discussion it is possible to suggest a fairly consistent mechanism for other reactions of active nitrogen with organic molecules that have been studied. The main features can be illustrated by comparison of the suggested mechanisms for propylene, the propyl chlorides, and propane. The observed products of these reactions can be explained if it is assumed that a chemically identical complex is formed in all the reactions:

$$N + C_3H_6 \rightarrow N.C_3H_6, \quad [26]$$

$$N + C_3H_7Cl \rightarrow N.C_3H_6 + HCl, \quad [27]$$

$$N + C_3H_8 \rightarrow N.C_3H_6 + H_2. \quad [28]$$

The differences observed are then ascribed to the increased stability of the complex in going from propylene to propane (the energy content of the com-

plex obviously decreases in that order), and to differences in ease of formation of the complexes. The formation of unsaturated hydrocarbons as secondary products can then be explained by calling on conservation of spin and the reluctance of molecular systems to transfer large amounts of internal energy into translational energy. Thus, a reaction scheme that can account for the unsaturated products from the propane and propyl chloride reactions is:

$$N + N.C_3H_6 \rightarrow C_3H_6^* + N_2 + (226 - E_1 - q) \text{ kcal.} \quad [29]$$

followed by[6]

$$C_3H_6^* \rightarrow C_2H_4^* + CH_2 + (E_1 - E_2 - 70) \text{ kcal.}, \quad [30]$$

or

$$C_3H_6^* \rightarrow C_2H_4 + CH_2^* + (E_1 - E_3 - 70) \text{ kcal.}, \quad [31]$$

and

$$C_2H_4^* \rightarrow C_2H_2^* + H_2 + (E_2 - E_4 - 42) \text{ kcal.}, \quad [32]$$

where q is the heat evolved in forming the $N.C_3H_6$ complex from N and C_3H_6 (derived from each reactant) and E_1, E_2, E_3, and E_4 are the excitation energies to reach the triplet states $C_3H_6^*$, $C_2H_4^*$, CH_2^*, and $C_2H_2^*$ respectively. If $C_2H_4^*$ is ethylene in a triplet state, the value of E_2 must be more than 90 kcal. (8) for reaction [32] to occur and it might be expected that the ratio of acetylene to ethylene formed would be much lower than that observed.

However, if, as seems reasonable, the structure of $N.C_3H_6$ is essentially

$$CH_3—CH—CH_2$$
$$\diagdown\ N\ \diagup$$

the most likely structure for $C_2H_4^*$ formed by reaction [30] should be $(CH_3—CH:)^*$, the ultimate fate of which will be determined by the relative probabilities of the spin-disallowed reactions

$$(CH_3—CH:)^* \rightarrow C_2H_4, \quad [33]$$
$$\rightarrow C_2H_2 + H_2. \quad [34]$$

It seems quite reasonable, then, that nearly equal amounts of acetylene and ethylene might be formed.

The value of E_1, hence the probability of reaction [30], should be quite sensitive to the extent of interaction between the nitrogen atom and the rest of the $N.C_3H_6$ complex. It might be expected to increase with increasing stability of the $N.C_3H_6$ complex, i.e. to increase from propylene to propyl chloride to propane. The amount of propylene formed by reaction [29] followed by

$$C_3H_6^* \rightarrow C_3H_6 \quad [35]$$

should therefore be greatest for propylene and least for propane.

In all the reactions, spontaneous decomposition of the complexes will also occur

$$N.C_3H_6 \rightarrow HCN + C_2H_5 \quad [36]$$

[6]*Spin-allowed reactions of the type*

$$C_3H_6^* \rightarrow C_2H_3 + CH_3,$$
$$C_3H_6^* \rightarrow C_3H_5 + H$$

might well occur, but these presumably would also lead to formation of unsaturated products.

followed by

$$N + C_2H_5 \rightarrow HCN + H + CH_3, \quad [37]$$
$$N + CH_3 \rightarrow HCN + 2H. \quad [2]$$

The C_2H_5 radicals formed in the propylene reaction should receive much more energy than those formed in the propyl chloride or propane reactions because of the relative energy contents of the complexes. Thus, it seems likely that the subsequent reaction

$$C_2H_5 \rightarrow C_2H_4 + H \quad [22]$$

might occur to a significant extent only in the propylene reaction, where it is probably responsible for most of the ethylene formed.

Both the formation of $N.C_3H_6$ complexes and their spontaneous decomposition should be slowest for propane, and somewhat, though probably not much faster for propylene than for the propyl chlorides. These considerations account for the formation of a much larger ratio of acetylene to ethylene in the C_2 products from propane and the propyl chlorides than from propylene, and for the formation of nearly as much propylene as ethylene in the propyl chloride reactions.

The reactions of the butanes and the cycloparaffins with active nitrogen may be treated in a manner entirely analogous to that outlined above, and discussion of them would seem to be superfluous.

The reactions for ethyl chloride corresponding to those for the C_3 molecules would be

$$N + N.C_2H_4 \rightarrow N_2 + C_2H_4^*, \quad [38]$$
$$C_2H_4^* \rightarrow C_2H_4, \quad [39]$$
$$C_2H_4^* \rightarrow C_2H_2 + H_2. \quad [40]$$

It seems reasonable that, for this reaction, $C_2H_4^*$ should be $(\dot{C}H_2-\dot{C}H_2)^*$, so that the spin-allowed reaction to form ethylene should be favored. Hence, much less acetylene than ethylene should be expected from the ethyl chloride reaction, and this is indeed observed. The small amount of acetylene formed might have resulted from the spin-allowed reaction

$$C_2H_4^* \rightarrow C_2H_2^* + H_2 \quad [41]$$

followed by

$$C_2H_2^* \rightarrow C_2H_2. \quad [42]$$

The reaction of ethane with active nitrogen yielded no ethylene or acetylene. It would appear, therefore, that a stable $N.C_2H_4$ complex (analogous to $N.C_3H_6$ from propane) is not formed. Nevertheless, the only reasonable mechanism for the direct reaction of ethane with nitrogen atoms is completely analogous to the corresponding ethylene and ethyl chloride reactions, viz.

$$N + C_2H_6 \rightarrow HCN + CH_3 + H_2 + 30 \text{ kcal.}, \quad [43]$$
$$N + CH_3 \rightarrow HCN + 2H. \quad [2]$$

The inference that the reaction

$$N + C_2H_6 \rightarrow N.C_2H_4 + H_2 + (q-33) \text{ kcal.} \quad [44]$$

does not occur seems reasonable. This reaction would be highly endothermic unless q, the binding energy of $N.C_2H_4$, is large, which must require a change

of spin. Ethane has fewer degrees of freedom than propane, and the lifetime of a collision complex with a nitrogen atom, and hence the chance for a change of spin during the collision, will be correspondingly reduced.[7] Thus, reaction [43] probably occurs as a straightforward spin-disallowed reaction. Unfortunately, the reaction with ethane appears to be complicated, since different activation energies were obtained in the low and high temperature ranges. It is possible (8) that there is a contribution from the indirect reaction

$$N_2\dagger + C_2H_6 \rightarrow N_2 + C_2H_5 + H \qquad [45]$$

followed by

$$N + C_2H_5 \rightarrow HCN + H + CH_3. \qquad [37]$$

With alkyl halides, which react rapidly with atomic nitrogen, the reaction analogous to [45] should be, for example,

$$C_2H_5Cl + N_2\dagger \rightarrow C_2H_5 + Cl + N_2. \qquad [46]$$

Since there was no evidence for the formation of significant amounts of atomic chlorine in any of the alkyl halide reactions, it seems safe to conclude that reactions of the type of reaction [45] are unable to compete with fast nitrogen atom reactions.

Since the reaction of active nitrogen with ethane showed a change of activation energy with temperature, there is a possibility that it is carried by hydrogen atoms in the manner demonstrated for the analogous reaction with methane, i.e.

$$H + C_2H_6 \rightarrow H_2 + C_2H_5 \qquad [47]$$

followed by nitrogen atom reactions with the alkyl radicals.

Acetylene and vinyl chloride behave similarly in their reactions with atomic nitrogen, and a chemically identical intermediate is probably formed in both reactions,

$$N + C_2H_2 \rightarrow N.C_2H_2, \qquad [48]$$

$$N + C_2H_3Cl \rightarrow N.C_2H_2 + HCl. \qquad [49]$$

Direct evidence for significant concentrations of $N.C_2H_2$ in the acetylene reaction is provided by the recovery of a polymer with a composition close to that expected for $(N.C_2H_2)_n$.

The heats of formation of CN, CH_2, etc., are not well enough established to permit any conclusions about the detailed mechanisms of these two reactions. The long lifetime of the $N.C_2H_2$ complex indicates that the spin-allowed reaction

$$N + C_2H_2 \rightarrow CN + CH_2^* - 12 \text{ kcal.} \qquad [50]$$

probably has a significant activation energy. On the other hand, similar production of HCN from acetylene and vinyl chloride by the spin-disallowed reaction

$$N.C_2H_2 \rightarrow HCN + CH - (q+6) \text{ kcal.} \qquad [51]$$

would seem improbable, since it would require that the heat of sublimation of

[7]*It is significant that ethyl chloride appears to be able to form the $N.C_2H_4$ complex. Owing to the presence of the heavy chlorine atom, the vibrational levels will be more closely spaced in ethyl chloride than in ethane and the chance of redistributing the collision energy among the internal degrees of freedom, and hence the collision lifetime, should be greater.*

graphite should be considerably less than the generally accepted value (170 kcal.), so that such a reaction would be exothermic even for $N.C_2H_2$ derived from vinyl chloride.

It is possible that most of the hydrogen cyanide production results from reactions of the type

$$N + N.C_2H_2 \rightarrow 2HCN + (218-q) \text{ kcal.}, \quad [52]$$

$$\rightarrow HCN + H + CN + (103-q) \text{ kcal.} \quad [53]$$

The reactions of methyl chloride, methyl cyanide, and methylamine, unlike the reaction of methane itself, appear to involve formation of relatively long-lived complexes. The observed increase in limiting yield of hydrogen cyanide with increase of temperature (7, 11, 14) can be explained if nitrogen atoms are destroyed by recombination catalyzed by the reactant; a quantitative treatment of the data for methyl cyanide on this basis gives good agreement with experiment (10). Recombination catalyzed by reactant should occur most readily if a complex is formed and should lead to side reactions. Thus, the reaction[8]

$$N + N.CH_3X \rightarrow N_2 + CH_3X \quad [54]$$

is exothermic by more than 200 kcal., and there should be a good chance that the CH_3X part of the complex should receive enough energy in internal degrees of freedom to dissociate into reactive fragments that can react very fast with atomic nitrogen, or among themselves to form the products such as cyanogen, acetylene, ethylene observed in the methyl chloride, methyl cyanide, and methylamine reactions.

The observed products of the methyl chloride reaction (7) clearly indicate that the primary reaction is

$$N + CH_3Cl \rightarrow HCN + HCl + H. \quad [55]$$

It seems likely that the main reaction responsible for hydrogen cyanide production in the methyl cyanide reaction [11] is similar, i.e.

$$N + CH_3CN \rightarrow 2HCN + H. \quad [56]$$

Thus, these two reactions probably resemble the ethylene reaction

$$N + C_2H_4 \rightarrow HCN + CH_3. \quad [1]$$

The analogous reaction with methylamine would be

$$N + CH_3NH_2 \rightarrow HCN + H + NH_2. \quad [57]$$

While the relation between ammonia production and methylamine flow rate (14) might be interpreted to indicate that ammonia is a primary product of the reaction, the amount of ammonia produced is only about one quarter the amount of hydrogen cyanide formed in the temperature range 84° to

[8] *By analogy with the unified mechanism, it may be expected that the intermediate complex would be formed by elimination of HX, e.g.*

$$N + CH_3Cl \rightarrow N.CH_2 + HCl.$$

This would still lead to catalyzed recombination and would, if anything, make it easier to understand the formation of C_2H_2 and C_2H_4 in the methyl cyanide and methylamine reactions. However, recovery of some methyl chloride even at the lowest flow rates used (7) indicates that elimination of HX is not essential for relatively stable complexes to be formed.

477°C. Hence, ammonia is probably not a primary product, and the primary reaction might well be analogous to that of ethane with nitrogen atoms, i.e.

$$N + CH_3NH_2 \rightarrow HCN + H_2 + NH_2 \quad [58]$$
$$(\text{cf. } N + C_2H_6 \rightarrow HCN + H_2 + CH_3).$$

This would suggest that the hydrogens of the NH_2 group, like those of the CH_3 group in ethane, make it difficult for transfer of an additional hydrogen to these groups.

Like methylamine, neopentane appears to resemble ethane in its reaction with atomic nitrogen. A primary reaction analogous to that suggested by the unified mechanism for saturated hydrocarbons of more than two carbon atoms would require the shift of a methyl group

$$C(CH_3)_4 + N \rightarrow (CH_3)_2C.CH.CH_3.N + H_2 \quad [59]$$

or elimination of methane instead of hydrogen,

$$C(CH_3)_4 + N \rightarrow (CH_3)_2C.CH_2.N + CH_4. \quad [60]$$

Neither process seems probable, and it is likely that the nitrogen atom attacks at a carbon–carbon linkage, as in ethane,

$$CH_3{-}\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}{-}CH_3 + N \rightarrow CH_3{-}\underset{\displaystyle CH_3}{\overset{|}{C}}{-}CH_3 + HCN + H_2 \quad [61]$$

followed by fast reaction of the C_4H_9 radicals to give more HCN and the unsaturated products observed.

The observed change in apparent activation energy with temperature might reflect a contribution from a reaction of the type

$$C(CH_3)_4 + N_2\dagger \rightarrow N_2 + C(CH_3)_3 + CH_3 \quad [62]$$

or perhaps the intervention of hydrogen atom attack, as with methane.

GENERAL DISCUSSION

One of the most interesting implications of the mechanisms suggested above is the ease of approach of the nitrogen atom to a completely shielded carbon atom, as in the alkyl chloride reactions. The theoretical approximation known as the "perfect pairing" approximation (9) should apply to the initial approach of a nitrogen atom. According to this approximation the interaction between the electrons in the outer orbitals of the nitrogen atom and those in the paired orbitals of the other reactant would give the usual coulomb and exchange terms, the former leading to attraction and the latter to repulsion. For *s*-electrons the exchange terms predominate, but for *p*-electrons the attractive coulomb terms are more important. Since the outer valence electrons of nitrogen, carbon, and chlorine are all *p*-electrons, it seems likely that the original approach of a nitrogen atom to an alkyl halide molecule will not be accompanied by a large increase in potential energy. Experimental confirmation of this is given by a recent study (33) of chlorine atom reactions in which, on the basis that the ease of approach depends on the electron affinities of the approaching particles, the relative activation energies for the

reactions of methane with Cl, H, and CH_3 are explained. This implies that the attractive forces result mainly from ionic structures in which electrons have shifted from the carbon bonds to the approaching radical.

When the nitrogen atom comes closer to the carbon atom, the approximation of perfect pairing would be expected to break down, and a better approximation would probably be given by delocalized molecular orbitals embracing nitrogen and carbon atomic orbitals, and either a hydrogen or a chlorine atomic orbital. Such a delocalization would result in the removal of at least part of the directional character of the carbon–hydrogen and carbon–chlorine bonds, and the decrease in potential energy accompanying the closer approach of the nitrogen atom to the carbon atom would be expected to offset most of the energy required to move the other atoms out of the way. From the valence bond point of view, this delocalization would be described as a contribution from several ionic structures involving, for example, a positive charge on a hydrogen atom and a negative charge on the nitrogen atom (corresponding to partial transfer of electrons from the C—H orbitals to the C—N orbitals). The tendency for a hydrogen atom to receive a positive charge would result in an attractive force between it and the polarizable chlorine atom, and it seems quite likely that one of the hydrogens and the chlorine atom would approach to form hydrogen chloride as both atoms were forced out of the way of the approaching nitrogen atom. Moreover, the loss of directional character, and perhaps also the tendency to form protons, should make it relatively easy for hydrogen shifts to occur as required by the unified mechanism presented previously. The directional character of carbon–hydrogen bonds is the basis for the conclusion of Rice and Teller (35) that direct attack at a completely shielded carbon atom requires a high activation energy. From the considerations given above, it appears likely that the directional character of such bonds will be lost on the close approach of a sufficiently electronegative radical.

If it is granted that there should be no large energy barrier in the reaction of nitrogen atoms with alkyl halides, it is interesting to consider whether a high rate of reaction implies little restriction to a change of spin. The main decrease in potential energy corresponding to delocalized orbitals will probably occur only after a pairing of spins (8), since the Pauli exclusion principle will allow lower orbitals to be occupied when more of the spins are paired. However, because of the attractive forces due to ionic structures mentioned above, it seems quite reasonable that collision between a nitrogen atom and an alkyl chloride molecule should lead to a complex with long enough lifetime to permit the change in spin to occur. To explain the marked effect of HCl on the recombination of hydrogen atoms, a stable H.HCl complex has been postulated (17). Nitrogen atoms should be able to form collision complexes of this type more readily than hydrogen atoms because of both their greater electronegativity and their greater mass. For a collision complex to have a reasonable lifetime, interaction between different vibrational modes of the complex is necessary, and this is favored by closer spacing of the vibrational energy levels, i.e. by greater mass of the atoms concerned.

Of the electronegative atomic reactants that have been studied, nitrogen atoms appear to be the only ones for which the direct attack is favored over hydrogen abstraction. This is probably due mainly to the endothermicity of reactions of the type

$$RH + N \rightarrow NH + R$$

and the high exothermicity of the direct attack.

APPENDIX

STANDARD HEATS OF FORMATION ($\Delta H°_f$) OF GASEOUS COMPOUNDS AT 25°C. FROM ELEMENTS

Formula	Remarks	$\Delta H°_f$ (kcal.)	Formula	Remarks	$\Delta H°_f$ (kcal.)
H		52.089	CH_3Cl		−19.6
H_2		0	CN		94
Cl		29.012	HCN		31.2
Cl_2		0	C_2H_2		54.194
HCl		−22.063	C_2H_4		12.496
N		113.0	C_2H_5		26
N_2		0	C_2H_6		−20.236
NH		86	C_2N_2		73.60
C		171.698	C_3H_6		8.5
C	Graphite	0.	C_3H_7	*n*-Propyl	24
CH		142.1	C_3H_7	Isopropyl	18
CH_2	Singlet	66	C_3H_8		−23.5
CH_2^*	Triplet	85	C_2H_3Cl		7.5
CH_3		32	C_2H_5Cl		−25.1
CH_4		−17.889	*n*-C_3H_7Cl		−31.1

Except as indicated below, the values were taken from National Bureau of Standards compilations (28, 29) or calculated from bond dissociation energies given by Steacie (38). For convenience, the temperature of reaction has generally been chosen as 25°C. For a few compounds, where values at 25°C. were not readily available, values for 0°K. have been used; the correction involved is less than the uncertainty in most of the values concerned.

$D(N_2)$: The high value, 9.76 ev., that is now generally accepted (cf. Ref. 8) has been used.

$\Delta H°_f(CN)$: Determinations of this quantity by several methods (4, 24, 27) indicate that a safe estimate is $\Delta H°_f(CN) = 94 \pm 2$ kcal.

$\Delta H°_f(CH_2)$, $\Delta H°_f(CH_2^*)$: The values recorded for these quantities are uncertain (see Ref. 38).

$D(CH_2—H)$: Estimates by several methods (20, 21, 26, 36, 51) indicate that $D(CH_2—H) = 86 \pm 5$ kcal.

Opinions differ (20, 52) as to whether the singlet or triplet state of the methylene radical is the more stable. It has been assumed that $D(CH_2—H)$ applied to formation of methylene radicals in the singlet state and, as a rough estimate, that 19 kcal. of excitation energy (24) is required to reach the triplet state.

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THE MICROPORE FLOW OF H_2O AND D_2O THROUGH ACTIVATED CARBON RODS[1]

By M. E. Huber,[2] E. A. Flood, and R. D. Heyding

ABSTRACT

The flow rates of water adsorbed on activated charcoal have been measured at temperatures between −24°C. and +35°C. and compared with the flow rate of adsorbed D_2O at 25°C. In earlier papers a formula was presented which describes the micropore flow rate of adsorbed water as a laminar flow of liquid adsorbate under a high pressure gradient due to surface forces. Our results confirm this picture. From our flow data the relative viscosity of adsorbates can be calculated. Above 0°C. the viscosity of the adsorbate shows nearly the same temperature dependence as liquid water; below 0°C. the viscosity increases much more rapidly, but there is no sudden increase which could be ascribed to freezing of an appreciable fraction of the adsorbate at any particular temperature. The greater temperature coefficient of the adsorbate viscosity is consistent with a viscous flow of liquid films over a solid surface which exerts attractive forces on the liquid.

INTRODUCTION

It has been well established (1, 3, 9) that in the absence of appreciable absorption, the flow of gases through active carbons is a viscous flow with slip through the macropore system. The flow rate may be described by the well-known equation

$$[1] \qquad K = \frac{Q_{pv}}{\Delta p} = A\sqrt{\frac{\overline{T}}{M}} + \frac{B}{\eta}\bar{p},$$

where Q_{pv} = flow rate in pv units,

$\bar{p}$ = mean of input and output pressures (mm. Hg),

A, B = constants,

M = molecular weight,

η = gas viscosity,

Δp = difference between input and output pressures.

From flow data for a gas such as helium the constants A and B can be evaluated and Equation [1] used to calculate flow rates of other gases of known viscosities at various temperatures, provided that the gases are not strongly adsorbed.

If a gas is strongly adsorbed the observed flow rates may be much higher than given by Equation [1]. Such increased flow rates have been attributed to flows through the micropore systems by (*a*) surface diffusion (2, 3, 4) and (*b*) laminar or viscous flow of liquid adsorbate. Previous work in this laboratory (8, 9) indicates that in the case of our carbon the second of these alternative mechanisms is the dominating one when the quantity adsorbed is at all large.

[1]*Manuscript received May 17, 1956.*
Contribution from the Division of Pure Chemistry, National Research Council, Ottawa. Issued as N.R.C. No. 4086.
[2]*National Research Council Postdoctorate Fellow 1954–55.*

If we assume that during the adsorption reaction the adsorbate and the adsorbent retain their own physical properties (equation of state) it can be shown (6, 7) that the adsorbate in order to be in equilibrium with the gas outside must have a volumetric mean pressure given by

$$[2] \qquad p_a = \int_0^p \frac{\rho_a}{\rho_g} dp = \left|\overline{\frac{\rho_a}{\rho_g}}\right| p;$$

p_a = volumetric mean pressure of adsorbate,

ρ_a = mean density of adsorbate,

ρ_g = gas density,

p = gas pressure.

Thus a small gas pressure difference across a carbon plug may give rise to a much larger pressure difference across the corresponding adsorbate. It has been shown (5) that these pressures actually exist and can be used to calculate dimensional changes of the solid with considerable accuracy (7).

Where gas densities are very low compared with liquid densities the flow rate of an adsorbate of uniform viscosity in micropore systems of uniform pore diameters is given by

$$[3] \qquad Q_m = -\frac{c}{\eta_a} \rho_a \frac{dp_a}{dz} = -\frac{c}{\eta_a} \frac{\rho_a^2}{\rho_g} \frac{dp}{dz}$$

or in integrated form

$$Q_m = -\frac{c}{L\eta_a} \int_{p_1}^{p_2} \frac{\rho_a^2}{\rho_g} dp = \frac{c}{L\eta_a} \left|\overline{\frac{\rho_a^2}{\rho_g}}\right| \Delta p,$$

where Q_m = flow rate in mass units,

C = constant (a function of pore dimensions),

η_a = viscosity of adsorbate (liquid viscosity),

L = length of carbon plug.

Assuming that the adsorbate has the viscosity of the corresponding liquid, it has been shown (9) that the micropore flow rates of benzene, ethyl chloride, diethyl ether, methanol, and water are described fairly well by Equation [3]. As a further check on the validity of Equation [3] we have measured the micropore flow rate of D_2O at 25°C. and the micropore flow rates of H_2O at temperatures from −24°C. to +35°C. The activated carbon rods or plugs through which the micropore flow rates were measured were similar to those used previously. We have also used carbon rods whose macropore systems were partially filled with a metal alloy, thus greatly increasing the relative contribution of the micropore flow to the total flow rate. Normally in measurements of the permeabilities of active adsorbents the observed flow is the total flow through both macropore and micropore systems. The "observed" micropore flow is obtained by calculating the macropore flow by means of Equation [1] and subtracting this calculated flow from the total. Evidently the smaller the relative contribution of the macropore flow the more accurately the micropore flow can be measured by such procedures. The experimental

results to date, while largely confirming the validity of Equation [3], indicate that the temperature coefficient of the viscosity of adsorbed water is higher than that of liquid water. The results are consistent with laminar flow of liquid films in a surface force field.

Experimental results and relevant discussion are presented in what follows.

EXPERIMENTAL

Material

The activated carbon consists of very uniform, zinc-chloride activated, extruded, and calcined rods of 0.38 dm. diameter. They come from the same supply as the ones described in earlier papers (9, 12), the carbon being very similar to National Carbon Co. N19. We repeat their properties:

Helium density	2.22±0.05 gm. per cc.
Hg density	0.707±0.001 gm. per cc.
Void fraction	0.68
Void fraction at saturation assuming adsorbate has density of liquid:	
diethyl ether	0.24
water	0.30
BET surface nitrogen	1100 meters^2 per gm.

Properties of Single Plugs

Plug	Length	Macropores filled to	N_2 flow at 35.3°C.	N_2 flow reduced by filling to	Micropore flow reduced by filling to
26	1.00	0%	$K = 0.00209\bar{p} + 0.62$	—	—
23	0.417	(36%)	$K = 0.104$	6.4%	67%
28	0.535	39%	$K = 0.102$	11.9%	71%
29	1.001	53%	$K = 0.023$	3.3%	—

Plugs 23 and 29 were filled with alloy for 20 min. at 220°C. and 340 p.s.i., then molded into indium at 195°C. with 340 p.s.i. Plug 28 was filled under the same conditions except that it was filled under 370 p.s.i. and molded into indium under 1 atm. (breaking the vacuum). The degree of filling of the macropores is calculated from the uptake of alloy (based on a macropore void volume of 0.30). For plug 23 this figure (36%) is evidently too small. Presumably during the molding some indium must have been taken up. Column 4 gives the K values for the nitrogen flow. For the filled plugs, only the slip part of Equation [1] is given because the other term is very small and our measurements are all at low pressures (<50 mm. Hg). Before the filling with metal, the K values per unit length were the same for all three plugs within 10%. The values of the last column are based on the micropore flow of plug 26.

Flow Apparatus

Fig. 1 illustrates the apparatus used for measuring the flow rates of water vapor through charcoal. The procedures used in obtaining the flow rates of

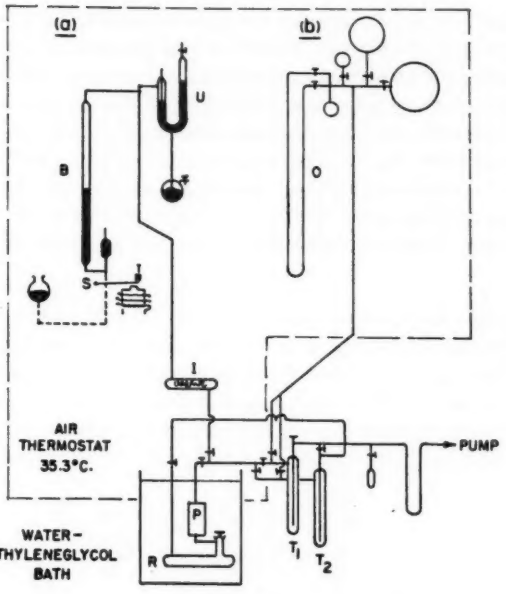


FIG. 1.

water vapor through plug 29 as well as the nitrogen flow rates through all of the plugs were essentially similar to those reported previously (12).

During the flow rate measurements for plugs 26, 23, and 28 the input sides of the carbons were exposed to saturated water vapor; this was done by keeping the reservoir R which contained liquid water at the same temperature as the plug. The gas flowing through the plug in the plug holder P was collected in one of the traps T. After a measured time, the trap was disconnected from the plug, and the amount of water in the trap determined in part (*b*) by expanding into a known volume and by reading the pressure on an oil manometer O. When the output pressure was zero, the traps were cooled with liquid nitrogen. For other output pressures, the traps contained a measured amount of water and were kept in a thermostat at the corresponding temperature. For a flow measurement under adsorption conditions, the plug was evacuated initially, equilibrated at the output pressure, and then the input pressure raised and Q_m or Q_{pv} observed till a constant value was obtained; for flow under desorption conditions, the plug was first saturated, the pressure reduced to a desired input pressure and equilibrated, the output pressure lowered, and Q_m observed as before.[3] The plug holder and the reservoir R were immersed in a water–ethyleneglycol bath, thermostated within ±0.01°C. For temperatures below 15°C., the thermoregulator controlled a pump which

[3] *Thus adsorption state flow rates are initially too high when measured from the input side (plug 29) and desorption flows too low, and conversely when measured on the output side (plugs 26, 23, and 28).*

circulates liquid from a reservoir cooled by mechanical refrigeration to a temperature a little below that desired in the thermostat. The nitrogen flows through the plugs were measured with the aid of part (*a*), Fig. 1.

The flow measurements for plugs 26, 23, and 28 were all reproducible within better than 5% while the more difficult measurements for plug 29 were usually reproducible within 10%. From time to time we repeated the nitrogen flow to make certain that no leaks had developed around the plug. Flow rates for plug 29 are given in *K* units while for plugs 26, 23, and 28, the flow rates are given in *pv* (mm. Hg×cc.) units per minute measured at 35.3°C.

Plug Holder

In runs with unfilled plugs the same type of holder was used as described previously (9, 12), the carbon rod being held between two funnel-shaped glass tubes and the sides surrounded with mercury, thus preventing gas flow around the carbon. When we used metal-filled plugs this holder was not satisfactory as the mercury amalgamates immediately with the low melting alloy in the plug. Fig. 2*a* illustrates the holder which was used in this case.

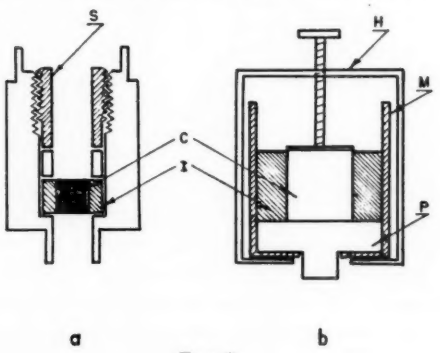


FIG. 2.

The carbon plug C is surrounded by a ring of indium I which fits precisely into the holder. By means of the screw S the indium, a very soft metal, is compressed and forms a tight seal. As indium picks up traces of mercury vapor very readily (11), the apparatus was kept free from mercury. The holder is connected with the glass system by glass to Covar seals. Fig. 2*b* shows the device used to make the indium ring around the plug. The carbon is held in the center of the cylinder by a screw. Then the whole is put in a bomb and indium is added. The bomb is evacuated overnight at 130°C. Then the temperature is increased to 190°C., the vacuum broken, and the desired nitrogen pressure applied for five minutes. The bomb is opened, the cylinder taken out, and after cooling down the piston is forced out.

The filling of the macropores with metal was carried out as follows. The plug was placed in a small test tube together with the Pb–Sn eutectic (61.8 Sn, 38.2 Pb, m.p. 183°C., *d*, 8.5 gm./cc.). The whole was placed in a bomb, which was evacuated overnight at 150°C.; then the temperature was slowly

increased to 220°C. At this temperature nitrogen pressure from a tank was applied for 20 min. It was found that this time was enough to fill the plug uniformly, as longer exposures to the pressure gave no more increase in weight. After the pressure was released the bomb was opened rapidly and the still liquid content of the test tube poured onto a glass plate. By this procedure no metal adheres to the surface of the carbon, hence from the increase in weight the volume occupied by metal can accurately be calculated.

The adsorption isotherm of the carbon was measured in a conventional McBain system. We found that the isotherm of a metal-filled plug was the same as of an unfilled one.

RESULTS

In order to compare our experimental results with the theory underlying Equation [3], it is convenient to modify the equation by putting $\rho_a = x/V$, where x = grams adsorbed per gram of carbon and V = micropore volume per gram of carbon, and also by putting $\rho_g = pM/RT$ and $p = \alpha p_s$, where p_s is the saturation pressure. With these substitutions Equation [3] becomes

$$Q_m = \frac{c}{L\eta_a}\frac{RT}{V^2M}\int_{\alpha_2}^{\alpha_1}\frac{x^2}{\alpha}\,d\alpha$$

$$= \frac{c}{L\eta_a}\frac{RT}{V^2M}\left|\overline{\frac{x^2}{\alpha}}\right|\Delta\alpha,$$

or in pv units

$$[3a] \qquad Q_{pv} = \frac{c}{L\eta_a}\frac{R^2T^2}{V^2M^2}\left|\overline{\frac{x^2}{\alpha}}\right|\Delta\alpha,$$

and in K units

$$[3b] \qquad K = \frac{Q_{pv}}{\Delta p} = \frac{c}{L\eta_a}\frac{R^2T^2}{V^2M^2}\frac{1}{p_s}\left|\overline{\frac{x^2}{\alpha}}\right|.$$

When pv is measured at a constant temperature (35.3°C.), but the porous adsorbent is at various temperatures, Equation [3a] can be written

$$[3c] \qquad Q_{pv}' = \frac{c'}{\eta_a}\frac{T}{M^2}\left|\overline{\frac{x^2}{\alpha}}\right|\Delta\alpha,$$

where $c' = cR^2T_{35}/LV^2$.

Equations [3a], [3b], [3c] permit of a number of searching experimental tests of their validity. Thus according to Equation [3b] at a given temperature the flow rate K, for a given vapor, should vary with the mean value of x^2/α averaged over $\Delta\alpha$, as obtained from the plot of x^2/α as a function of α. Also for equal values of $|\overline{x^2/\alpha}|$, K values at 25°C. and 35°C. should be related as follows:

$$\frac{K_{25}}{K_{35}} = \frac{\eta_{35}}{\eta_{25}}\left(\frac{T_{25}}{T_{35}}\right)^2\frac{p_{s(35)}}{p_{s(25)}},$$

where η_{35} and η_{25} are the viscosities of the adsorbate at 35°C. and 25°C. respectively, $p_{s(35)}$ and $p_{s(25)}$ are the corresponding saturation pressures, and T_{35} and T_{25} are the absolute temperatures.

While in the theory underlying these equations, the adsorbate layers are assumed to have the viscosity of the normal liquid, the "viscosity" of a Newtonian liquid in a strong attractive force field will be greater than that of the normal liquid and show a greater temperature dependence, such effects being the greater the thinner the liquid layer. Thus the adsorbate in the desorption state should have a viscosity somewhat closer to that of the normal liquid than the adsorbate in the adsorption state.

In the case of H_2O micropore flow, assuming that the adsorbate has the viscosity of liquid water, the ratio $K_{25}/K_{35} = 1.34$. Fig. 3 shows plots of K values for H_2O at 25°C. and 35°C. as functions of $\bar{\alpha}$ (i.e., of $(p_1+p_2)/2p_s$)

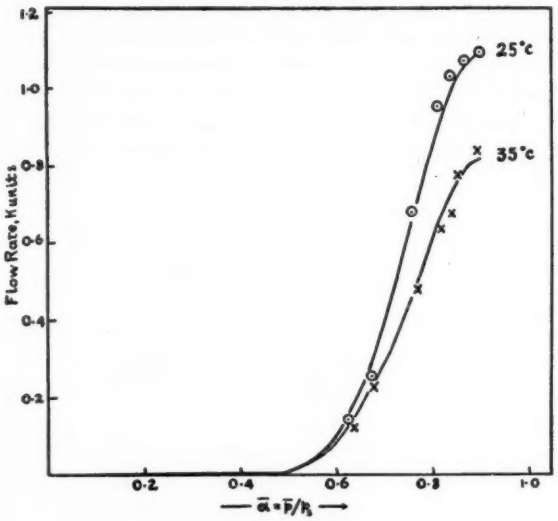


FIG. 3.

where $\Delta\alpha$ is 0.2 in each case. The solid lines are calculated from the observed K value at 25°C. and $\bar{\alpha} = 0.89$. The isotherm is used to calculate K at other values of $\bar{\alpha}$ and K_{25}/K_{35} is taken as 1.34. The experimental points are indicated by the crosses.

The agreement between the observed and calculated values is probably well within the experimental error since it is difficult to set and maintain $\Delta\alpha = 0.2$ exactly for each value of $\bar{\alpha}$.

While these equations are based on thermodynamic equilibrium between vapor and adsorbate and hence, strictly, can be valid only for infinitesimal $\Delta\alpha$, it is much easier experimentally to measure flow rates from $\alpha_1 = 1$ to $\alpha_2 = 0$ (i.e., from saturation to vacuum) than it is to set, maintain, and measure the slow flow rates for small values of $\Delta\alpha$. This procedure is a much more stringent test of the practical validity of these equations.

Since as shown by Coolidge (5) the adsorption isotherm of water vapor expressed as a function of the relative pressure, α, is the same over the tem-

perature range −30°C. to +30°C., then for $\Delta\alpha = 1$, $\overline{|x^2/\alpha|}$ has the same value in this temperature range. Accordingly, if our equations are valid under these conditions, we should have from Equation [3c]

$$\frac{Q'_{pv(T_1)}}{Q_{pv(T_2)}} = \frac{\eta_{l(T_2)} \cdot T_1}{\eta_{l(T_1)} \cdot T_2}$$

where $Q'_{pv(T_2)}$ is the flow rate in pv units at the plug temperature T_2, the volumes being measured at some constant temperature (35.3°). $\eta_{l(T1)}$ is the viscosity of liquid water at T_1. This relation should hold over the temperature range −30° to +30°C., provided that the adsorbate does not freeze and has the viscosity of water.

In Table I the micropore flow rates for plug 28 are given at 25°C. and at 15°C. and their ratios compared for various values of $\Delta\alpha$ for both adsorption

TABLE I

MICROPORE FLOW RATES OF WATER VAPOR THROUGH PLUG 28 AT 25°C. AND 15°C.

	α_1	α_2	Q(25°C.)	Q(15°C.)	Q_{25}/Q_{15}	Q_{25}/Q_{15} calc.
Adsorption state	1	0.00	25.1	16.7	1.50	1.32
	1	0.50	23.5	15.2	1.55	1.32
	1	0.80	16.6	10.8	1.54	1.32
Desorption state	1	0.00	45.3	33.3	1.36	1.32
	1	0.80	17.3	12.6	1.37	1.32

and desorption states. The calculated curves are shown in Fig. 4 based on the adsorption flow rate for $\Delta\alpha = 0.2$.

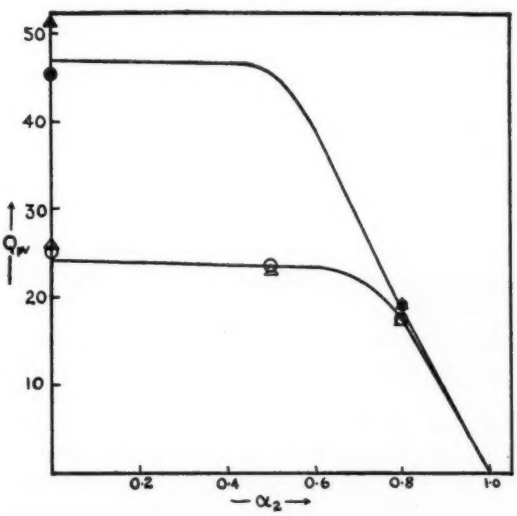
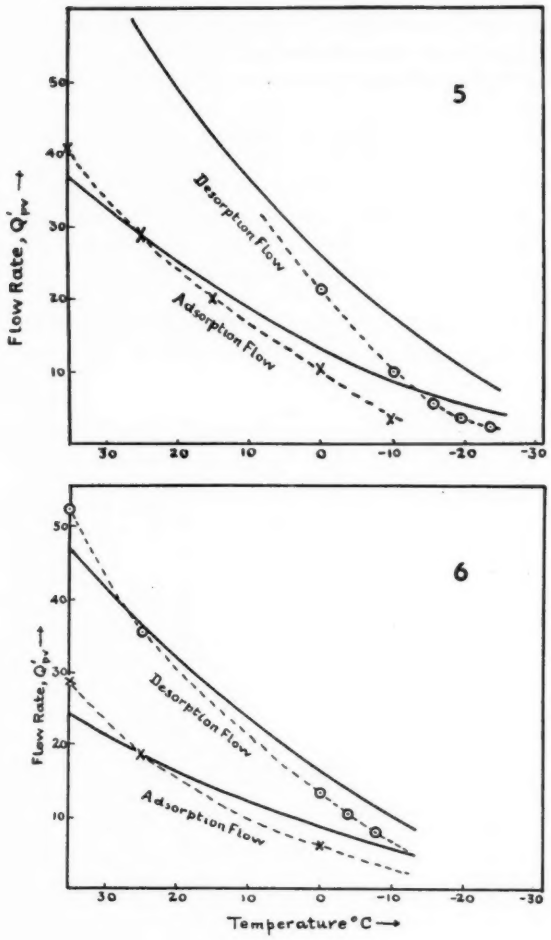


FIG. 4.



FIGS. 5 and 6.

Evidently Equation [3] is reasonably valid for $\Delta\alpha = 1$ as well as for $\Delta\alpha = 0.2$ or less.

In Figs. 5 and 6 observed values of $Q_{pv}'(\Delta\alpha = 1)$ for plugs 23 and 26 respectively for both adsorption and desorption states are plotted as functions of the temperature. The solid lines are calculated from the value of Q_{pv}' at 25°C. under adsorption conditions. If the equations are valid the ratios of the Q_{pv}' values for plugs 23 and 26 should be independent of temperature and that this is practically the case is shown by the data in Table II.

It will be noted that if the adsorption isotherm expressed as moles adsorbed (i.e. x/M) is the same for two gases, as is the case with H_2O and D_2O (cf.

TABLE II

MICROPORE FLOW RATES OF H_2O THROUGH PLUG 26 (UNFILLED) AND PLUG 23 (METAL FILLED) AT VARIOUS TEMPERATURES WHEN $\alpha_1 = 1$ AND $\alpha_2 = 0$
(Values in brackets are interpolated)

Temp., °C.	Q(plug 23)		Q(plug 26)		Q_{23}/Q_{26}	
	Ads.	Des.	Ads.	Des.	Ads.	Des.
35.0	40.5		28.9	52.4	1.39	
25.0	28.8		18.5	35.5	1.57	
15.0	20.0					
0.0	10.5	21.6	6.43	13.58	1.63	1.59
−3.8		(16.8)		10.4		1.61
−7.7		(12.3)		8.0		1.54
−9.7		9.9				
−10.0	3*					
−15.4		5.5				
−19.2		3.9				
−23.6		2.56				

**Q not quite constant, rising slowly even after eight days. Highest observed value 2.9.*

TABLE III

MICROPORE FLOW RATES OF H_2O AND D_2O AT 25°C., PLUG 28, ADSORPTION STATE

α_1	α_2	Q_{H_2O}	Q_{D_2O}	Q_{H_2O}/Q_{D_2O}	η_{D_2O}/η_{H_2O}
1	0.00	25.1	18.2	1.38	1.23
1	0.80	16.6	12.3	1.35	1.23

Fig. 7), then at the same temperature the ratios of Q_{pv}' for such pairs are inversely proportional to the ratios of their liquid viscosities. In Table III the observed micropore flow rates of D_2O and H_2O are compared. Evidently the observed ratio is somewhat higher than the ratios of the normal viscosities of D_2O and H_2O. It may be remarked that it is easily shown that in order that the D_2O and H_2O isotherms be related as found in Fig. 7, the molar adsorption potential for D_2O must be higher than that of H_2O, and hence the ratio of the viscosities of the liquids in these surface fields greater than their ratio in the absence of such fields, i.e., greater than the ratio of the normal viscosities of D_2O and H_2O.

DISCUSSION

The experimental evidence presented above largely confirms the validity of the underlying theory and indicates that the adsorbate behaves essentially as a liquid film in a force field, and that at temperatures above 0°C. the adsorbate viscosity is essentially that of the normal liquid. The experimental evidence indicates that the integrated equation is also valid even for the range $\alpha_1 = 1$, $\alpha_2 = 0$, i.e., $\Delta\alpha = 1$.

The theory underlying the flow equation is based on the assumption that equilibrium, as between adsorbate and vapor, exists everywhere throughout the flow path. Thus the basic equation is

$$-Q_{pv} = A\sqrt{\frac{T}{M}}\frac{dp}{dz} + \frac{B}{\eta_g}p\frac{dp}{dz} + \frac{c}{\eta_1}\frac{\rho_s^2}{\rho_g}\frac{dp}{dz},$$

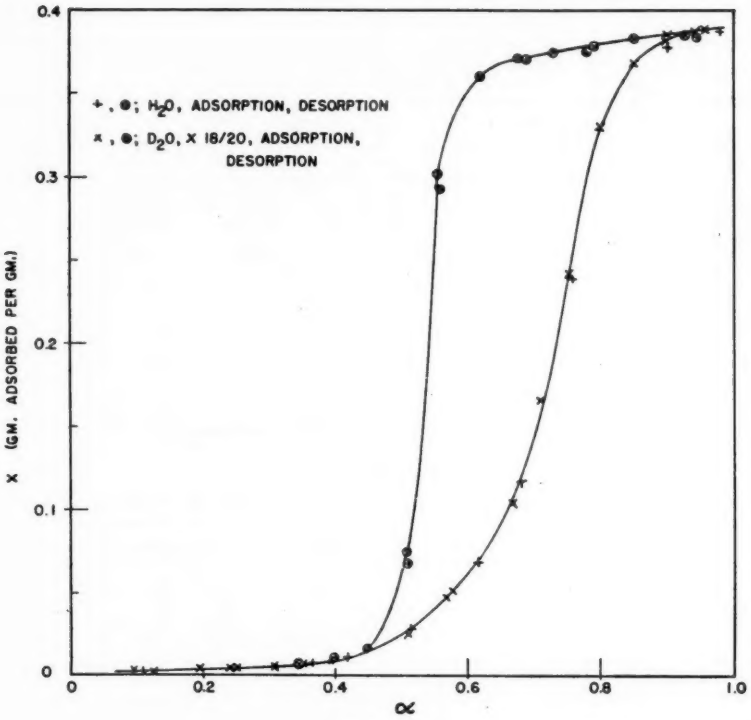


FIG. 7.

where η_g is the gas viscosity, η_l the liquid viscosity, etc. The first two terms of the right-hand member of the equation apply to the macropore system, and the third term to the micropore system. For small B and p the integrated form may be written

$$Q_{p_s} = \frac{A}{L}\sqrt{\frac{\overline{T}}{M}}\cdot p_s + \frac{c}{L\eta_l}\left|\frac{\overline{\rho_s^2}}{\rho_g}\right| p_s.$$

It may appear very surprising that this equation should hold even approximately, since at the low surface coverages near the effluent end of the rod where $p \rightarrow 0$, the traction of the adsorbed layer over the solid surface must be very different from that between water layers. Thus at first sight one might expect little direct correlation between liquid viscosity and flow rate when $\Delta\alpha = 1$.

While mathematically the integration carried out above is equivalent to treating the two pore systems as though they were independent, these systems are not physically independent. In the case of two physically independent systems the gas pressure gradient in the macropore system, neglecting the small Poiseuille term, would be linear, while the equilibrium gas pressure gradient corresponding to the micropore flow would be quite different conforming to

the condition that $(c/\eta_l)(\rho_a^2/\rho_g)(dp/dz)$ on the input and output ends be the same, i.e., to constancy of Q_m (micropore). For macropore and micropore flows, the corresponding "equilibrium" gas pressures expressed as fractions of saturation, or α, are shown in Fig. 8 as functions of the distance z along the plug. As both systems are closely interconnected everywhere, only one gas pressure gradient can exist. Thus the form of $\alpha(z)$ for the actual system will lie somewhere between the macropore and micropore curves shown, depending on the relative permeabilities of the two pore systems. Evidently the flow through

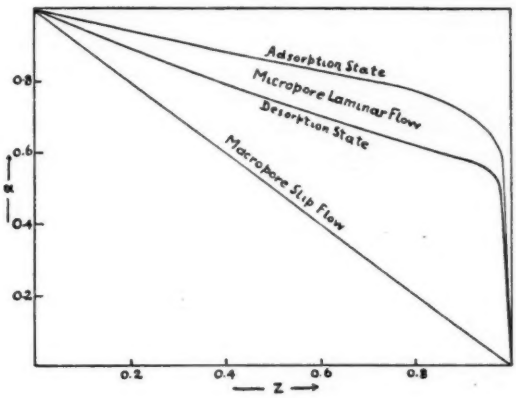


FIG. 8.

either one of the pore systems is not constant along the flow axis. For the case illustrated relatively more water flows through the micropores on the input side than on the output side. If ρ_a were constant along the flow axis, as would be the case if the micropore system were liquid filled from end to end, and quasi-equilibrium at the two ends maintained by surfaces of different curvatures (a model desorption state) the micropore flow would be relatively greater on the output side.

Fig. 8 shows that for micropore flow, when $\alpha_1 = 1$ and $\alpha_2 = 0$, i.e., from saturation to vacuum, the whole carbon is nearly saturated (92% and 88% saturated for desorption and adsorption states, respectively). Thus the steady state is reached much sooner for desorption flow than for adsorption flow. At -10°C. the steady state of flow under desorption conditions was reached in a day but for adsorption flow even after eight days the flow rate was not quite constant.

That the flow should be inversely proportional to liquid viscosity, in spite of the fact that at the low pressure end of the plug the theoretical model cannot be even approximately valid, is made clear from Fig. 8. Evidently 95% of the length of the flow path is nearly saturated, practically all of the equilibrium gas pressure drop occurring over the last 5% of the length. If the viscosity in the last 5% were twice as large as in the rest of the plug, the pressure drop over the 5% must be twice as large as shown in Fig. 8. Thus the

pressure gradient which forced the adsorbate through 95% of the length of the carbon has, in this latter case, to force it through 97.5% of its length. The total effect on the flow rate is less than 3%. Evidently the apparent viscosity of the adsorbate at the effluent end of the carbon rod does not influence the flow rates materially when the influent end is saturated.

If the micropore flow rates are much too high for equilibrium between adsorbate and gas pressures (input and output) to be even approximately attained (e.g. a very short plug or thin diaphragm) serious departures from the above equations are to be expected. In such cases the density of the adsorbent at the effluent end will be much too great and the adsorbate pressure gradient too small, the former leading to larger Q_m values than calculated, the latter to smaller values. Such high flow rates are also liable to cause a temperature gradient across the plug and lead to lower Q_m values.

Finally in Fig. 9 apparent adsorbate viscosities are plotted as functions of temperature. Evidently, there is no evidence of freezing of any considerable part of the adsorbate. Since in the desorption state part of the adsorbate is

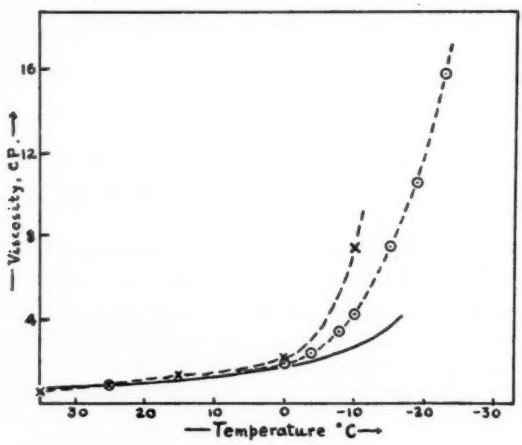


FIG. 9.

under a net negative pressure, one might have expected more evidence of solidification for desorption state flow. However, no such evidence can be adduced from the data. Assuming (10) that one may write $\eta = B\exp(E_{vis}/RT)$, the mean "activation energy", E_{vis}, of viscous flow for liquid water in the interval +35°C. to 0°C. is of the order of 4.3 kcal. For desorption flow E_{vis} is of the order of 4.9 kcal. while for adsorption flow it is about 6.0 kcal. If the "potential" of the surface regions containing the "liquid" films is 3 or 4 times ΔE_{vis}, i.e. similar to the relation of E_{vis} to E_{vap} for normal liquid water, the surface potential is about 5 kcal. per mol. adsorbed for the adsorption state and about 2 kcal. for the desorption state. These surface "energies" are about what one might expect for such carbons.

The evidence presented above indicates that for our carbon rods the micropore flow rate of water can be described semiquantitatively by the equation

$$Q_m = \frac{c}{L\eta_1}\int_{p_2}^{p_1} \frac{\rho_a^2}{\rho_g}\, dp.$$

The viscosity of the adsorbate appears somewhat higher than that of liquid water and the temperature coefficient of the adsorbate viscosity greater. The equation appears to describe the relative flow rates for various values of $\int_{p_2}^{p_1} \rho_a^2/\rho_g\, dp$ at constant temperature more accurately than it describes the relative flow rates at constant $\int_{p_2}^{p_1} \rho_a^2/\rho_g\, dp$ values and varying temperatures. The variation of the viscosity of the adsorbate is qualitatively in accordance with theoretical considerations.

It is, of course, to be emphasized that the micropore flow mechanisms discussed here are not applicable to systems of micropores of molecular dimensions as no laminar flow can take place in pore systems of only one or two molecular diameters. However, the equations should be reasonably valid as applied to the flow of five or more molecular layers and hence should be reasonably valid as applied to the flow of small molecules adsorbed in micropore systems of almost constant pore sizes of 10 Å diameter or more. In the case of micropore systems of platelet structure, the distance between platelets might be somewhat less than 10 Å and still be consistent with liquid viscous flow.

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THE CHEMICAL STABILITY OF THE *S*-METHYL XANTHATES OF SOME SIMPLE ALCOHOLS[1]

By D. L. Vincent[2] and C. B. Purves

ABSTRACT

n-Octadecyl *S*-methyl xanthate, m.p. 38–39°, and *n*-hexadecyl *S*-methyl xanthate, m.p. 28–28.5°, were prepared for the first time, and were used to study the behavior of the *S*-methyl xanthate group toward reagents commonly used in research on carbohydrates. Although stable to some conditions of acetylation, hydrolysis, and methanolysis, the *S*-methyl xanthate group was destroyed by all methylating agents tried, with the exception of nitrosomethylurethane. The latter reagent converted a sodium xanthate salt in high yield to the *S*-methyl ester. Octadecyl and hexadecyl *S*-methyl xanthates when oxidized with hydrogen peroxide yielded crystalline substances of composition $C_{20}H_{40}O_4S_2$ and $C_{18}H_{36}O_4S_2$, respectively, whose structures were not determined. These substances each contained three additional oxygen atoms. Various attempts to estimate the *S*-methyl xanthate group by oxidation with bromine or periodic acid, or by reduction to methyl iodide, were unsuccessful.

INTRODUCTION

As a preliminary to research on xanthates of carbohydrates, it seemed desirable to investigate some simple, crystalline derivative of the xanthate group that was more stable than a free xanthic acid or its alkali salt toward reagents frequently used in carbohydrate chemistry. Xanthate-*S*-methyl esters at once came into consideration, because they could be formed in high yield by the action of methyl iodide on a suitable salt. The term "xanthate ester" referred to a double ester such as $C_2H_5OCSSC_2H_5$, whose formal name was ethyl ethoxymethanethionothiolate, but which could be more clearly described as *O*-ethyl *S*-ethyl xanthate (6).

Simple xanthate esters were usually high-boiling liquids, and of the *S*-methyl compounds only eight were reported as crystalline. All eight were derived from aromatic, hydroaromatic, and terpene alcohols, and their carbon skeletons were unnecessarily complicated for the purpose in view. Nevertheless, the *S*-methyl xanthates of benzyl and hexahydrobenzyl alcohol, and of menthol, were prepared for reference purposes. Whitmore and Simpson's modification (25) of the long-neglected Zeise (27) "one-step" process employing the alcohol, solid sodium hydroxide, carbon disulphide, and later methyl iodide, was used. The melting point of the hexahydrobenzyl derivative was confirmed as 16.5°, apparently the value given by Aleksandrovich (1), and not as 165°, as misquoted by Chemical Abstracts and British Chemical Abstracts. The same general method was used to synthesize several *S*-methyl xanthates of normal aliphatic alcohols in 60–80% yield. It transpired that the octyl derivative was a liquid, and that the *S*-methyl xanthates of *n*-hexadecyl (cetyl) and *n*-octadecyl (stearyl) alcohol were crystalline solids whose melting

[1]*Manuscript received May 28, 1956.*
Contribution from the Division of Industrial and Cellulose Chemistry, McGill University, and from the Wood Chemistry Division, Pulp and Paper Research Institute of Canada, Montreal, Que. Abstracted from a Ph.D. thesis submitted to the University by D. L. V. in March 1953.
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points were in a practical range. Most of the subsequent work was carried out on the higher-melting octadecyl derivative, but even in this series recrystallizations of the wax-like solids had to be performed in a room at 8°, and often occasioned serious losses in yield.

There are several assumptions in the literature that a sodium xanthate salt in presence of an excess of nitrosomethylurethane yielded the methyl ether of the parent alcohol. When a solution of sodium octadecyl xanthate (80–87% purity) in methanol was mixed with a fivefold molar excess of the above reagent, *O*-octadecyl *S*-methyl xanthate, and not the expected methyl ether of octadecanol, was swiftly formed in quantitative or nearly quantitative yield. Diazomethane was probably the actual methylating agent because the solution became yellow as the nitrosomethylurethane was added. In the same way, crude potassium benzyl xanthate gave benzyl *S*-methyl xanthate, although manipulative and other difficulties greatly reduced the yield.

Table I summarizes experiments on the stability of various *S*-methyl xanthates toward alcoholic sodium hydroxide. Distinct end points to phenol-

TABLE I

SAPONIFICATION OF *O*-OCTADECYL *S*-METHYL XANTHATE IN 90% AQUEOUS ETHANOL[a]

Conditions	Hydrolysis, %	
	NaOH, 1.2 *N*	NaOH, 0.09–0.11 *N*
1 hr. near 20°	19.9	4.1
48 hr. near 20°	78.9	75.0
1 week near 20°	161	175
15 min. at reflux[b]	73.7, 68.8	68.7
30 min. at reflux	92.5, 89.3	92.1
1 hr. at reflux[c,d]	99.7, 102	99.2, 98.5

[a] *The pure samples, 0.19–0.32 gm., were dissolved in 5 ml. or 10 ml. of 1.2 N alkali, or in 50 ml. of the 0.1 N alkali.*

[b] *When heating was preceded by 90 min. at 20° and with 0.8 N potassium hydroxide, the hydrolysis of benzyl S-methyl xanthate was 101, 102%.*

[c] *Hydrolysis of benzyl S-methyl xanthate, 91, 100, 84%. End points indistinct.*

[d] *Hydrolysis of menthyl S-methyl xanthate 80–100%. End point very indistinct.*

phthalein were obtained when saponifications of *O*-octadecyl *S*-methyl xanthate were titrated with standard hydrochloric acid, but those given by benzyl *S*-methyl xanthate were somewhat transitory. The assumption that complete hydrolysis corresponded to the reaction $R—OCSSCH_3 + 2NaOH \rightarrow R—OH + Na_2CO_2S + CH_3SH$ usually gave good results when the solution was boiled, but not when saponifications were carried out at room temperature and failure to expel methyl mercaptan led to an overconsumption of alkali. Decinormal alkali was almost as effective as *N* sodium hydroxide. In one experiment a 97% yield of nearly pure octadecanol was recovered, and in others the recoveries of benzyl alcohol and menthol were both about 70%. On the other hand, boiling 25% aqueous sodium hydroxide left over 95% of the *O*-octadecyl *S*-methyl xanthate unchanged after two hours. These results supplemented McAlpine's observation (17, 18) that concentrated alcoholic potassium

hydroxide caused complete hydrolysis of menthyl *S*-methyl xanthate in 12 to 18 hr., but that this substance, as well as its bornyl analogue, was stable to boiling 40% aqueous potassium hydroxide. Lieser and Leckzyck (16), however, found that an *S*-methyl xanthate of methyl glucoside was readily hydrolyzed by aqueous alkali. To sum up, it appeared likely that xanthate esters resisted decomposition by aqueous alkali when they were highly insoluble in this medium, but in other circumstances were far less stable to alkali than their sodium salts. Neither the ester nor the salt was likely to survive the conditions usual for methylating carbohydrates with dimethyl sulphate and alkali. Deacylation with *N* aqueous alcoholic ammonia might be possible without disturbing *S*-methyl xanthate groups, because the octadecyl derivative was stable to this reagent at room temperature for days. Nevertheless, Laakso (14) and earlier workers found that xanthamides (thiourethanes) resulted when xanthate esters were treated with aqueous or alcoholic ammonia. *O*-Octadecyl *S*-methyl xanthate was also nearly stable to pyridine at room temperature, although decomposition was extensive when the solution was heated (17, 18).

Lieser and Leckzyck (16) remarked that their *S*-methyl xanthate of methyl glucoside was surprisingly stable to boiling dilute hydrochloric acid. This contrast to the instability of xanthate salts toward acid was emphasized by the behavior of *O*-octadecyl *S*-methyl xanthate, which was not appreciably affected by boiling 6 *N* hydrochloric acid for three hours, and was recovered in high yield after exposure to the 43% acid for 24 hr. at 0°. Neither heating under reflux, nor in a sealed tube at 120°, with 3% methanolic hydrogen chloride caused appreciable change within three days, but decomposition was extensive when the temperature was raised to 160° during six days. This decomposition might have originated in thermal effects, because the pure xanthate ester decomposed vigorously and exothermally at 180–190°. By analogy with the behavior of other xanthate esters, the heating might have produced either a modification that was more stable thermally (6, 17, 18) or an isomerization to a dithiocarbonate, RSCOSR (12, 14), or the well-known Chugaev breakdown to an unsaturated hydrocarbon (2, 8, 25). The results in general suggested that the *S*-methyl xanthate group was reasonably stable to conditions often used for the hydrolysis and methanolysis of carbohydrates. This stability extended to acetylation or acetolysis with acetic anhydride and zinc chloride, as Lieser and Leckzyck (16) were aware.

A few experiments on the stability of *O*-octadecyl *S*-methyl xanthate toward heavy metals and their salts were carried out with the object of discovering mild conditions for dexanthation. When an alcoholic solution of the ester was heated under reflux with silver oxide or silver carbonate for at least one hour, octadecanol was formed together with a considerable amount of lower-melting material. Silver nitrate and mercuric acetate promoted chemical change at room temperature, but the major product was not octadecanol; cadmium carbonate failed to react with an ether solution of the xanthate within two weeks. Lieser and Leckzyck (16) employed silver or mercury salts to recover methyl-α-glucoside from its *S*-methyl xanthate, and their use in removing

sulphur from other types of organic compounds is well known. A solution of thallous ethylate in dry benzene reacted readily with *O*-octadecyl *S*-methyl xanthate, giving a high yield of octadecanol and a black precipitate of thallium sulphide (or sulphides) within 12 hr. at room temperature. These experiments showed that any *S*-methyl xanthate groups present in a carbohydrate would be removed during methylation with silver oxide and methyl iodide, or with thallous ethylate followed by methyl iodide (21). It might, however, prove possible to remove such groups without disturbing any acetyl groups in a partly acetylated substance.

Some years ago Fletcher (11) found that *O*-ethyl *S*-(tetraacetyl-D-glucopyranosyl)-xanthate was desulphurized in high yield to tetraacetyl-1,5-anhydro-D-sorbitol when boiled in alcohol with Raney nickel. The same reagent

$$C_2H_5OCS_2—C_{14}H_{19}O_9 \rightarrow C_{14}H_{20}O_9$$

enabled Baddiley (4) to obtain phenylethane from methyl phenyl dithioacetate

$$C_6H_5CH_2CS_2CH_3 \rightarrow C_6H_5CH_2CH_3.$$

These results suggested that methane and octadecanol might be produced in a similar way from *O*-octadecyl *S*-methyl xanthate. The product, however, consisted of only 50–65% of octadecanol (m.p. 58°), and a white wax melting at 28–31.5° which could not be adequately purified by recrystallization, and whose relative amount increased to about 60% when the desulphurization was carried out at room temperature. The substance was a mixture which might have contained a little octadecyl methyl ether (m.p. 30–31°).

Although Delépine (9) observed that simple xanthate esters often oxidized spontaneously in air with the evolution of light and fumes, and were chemiluminescent, Billeter and Wavre (5) were apparently the only workers to identify products from a similar oxidation. They found that in presence of aqueous ammonia *O*-methyl *S*-methyl xanthate absorbed oxygen quickly and that sulphuric, sulphurous, and thiosulphuric acids were formed; *O*-ethyl *S*-ethyl xanthate yielded *O*-ethyl *S*-ethyl thiocarbonate in the same circumstances. On the present occasion, *O*-octadecyl *S*-methyl xanthate was oxidized with an excess of 30% hydrogen peroxide, an agent often used to prepare sulphones from thioethers. The product consisted of a white, crystalline substance whose composition, $C_{20}H_{40}O_4S_2$, indicated that three oxygen atoms had been added to the original xanthate molecule with the retention of both sulphur atoms. The substance was stable to acid and when saponified yielded octadecanol, hydrogen sulphide, and no sulphate ion. A similar oxidation of *O*-hexadecyl *S*-methyl xanthate yielded a crystalline compound, $C_{18}H_{36}O_4S_2$, also containing three extra oxygen atoms, but a preliminary oxidation of benzyl *S*-methyl xanthate resulted in a mixture of products including benzyl alcohol. A detailed examination of these interesting oxidations was deferred.

Some unsuccessful attempts were made to determine the *S*-methyl xanthate group by titrating an acidified solution of the octadecyl derivative with potassium bromide – potassium bromate, essentially as described by Siggia and Edsberg (22) for the oxidation of thioethers to sulphoxides. Both sulphur

atoms in the xanthate ester, however, were oxidized beyond the sulphoxide stage to an extent depending on the conditions, and the end point was indistinct. Liquid bromine readily oxidized octadecyl *S*-methyl xanthate to a white wax which contained neither sulphur nor halogen, and which was neither stearaldehyde nor stearic acid. Oxidations of the *S*-methyl xanthate with paraperiodic acid (another reagent of value in carbohydrate chemistry) also proceeded to an indefinite end point and failed to provide a basis for an analytical method. Several attempts were made to devise a method of analysis for the methylthio group (—SCH_3) in xanthate-*S*-methyl esters by cleavage to methyl iodide with constant-boiling hydriodic acid. Use was made of the Vieböck and Schwappach (23) method for methoxyl groups, in which the methyl iodide was absorbed in a solution of bromine, and of the Kirpal–Bühn (13) modification with pyridine as the absorbing agent. This modification was particularly suitable for substances containing sulphur. Both procedures, however, failed to account for more than a small fraction of the methylthio group, even when the boiling with hydriodic acid was prolonged for several hours. This result explained why Lieser and Leckzyck (16) were able to determine the methoxyl content of a xanthate-*S*-methyl ester of methylglucoside without much interference from the methylthio unit. In an earlier article (15), however, Lieser attempted to determine the methylthio group in a supposed cellulose xanthane-*S*-methyl ester by the same procedure, and attributed the unexpectedly low result to the occurrence of side reactions during the preparation of the ester.

EXPERIMENTAL

Materials

At room temperature, the solubilities of octadecanol in ligroin (b.p. 30–50°), benzene, acetone, ethanol, methanol, and ethanol–water (3:1) were approximately 1.25, 3.85, 2.2, 1.7, 0.7, and 0.2% respectively; well-formed leaflets were obtained from ligroin, but the crystal habit deteriorated progressively through the above list of solvents. Both octadecanol and hexadecanol were purified from ligroin. Absolute ethanol, methanol, and ether were purified by standard methods. The *S*-methyl xanthate of benzyl alcohol was prepared by Whitmore and Simpson's method (25) employing solid sodium hydroxide, and the product, isolated in 70% yield, melted correctly at 28.5–29.5° (20). The same general method was used, apparently for the first time, in the preparation of the *S*-methyl xanthates of hexahydrobenzyl alcohol and of menthol, although xanthation occurred somewhat less readily in the latter case. Yields were 30% and 32%, and melting points were correct at 16–17° (1) and 38.5–39° (8), respectively. Determinations of sulphur were made either by the semimicro Carius method, or by the method of Waters (24), which employed bromine and nitric acid at atmospheric pressure as the oxidizing agent.

O-Hexadecyl S-Methyl Xanthate

Pure hexadecanol, 36.3 gm. (0.15 mole), was dissolved in 200 ml. of reagent grade carbon disulphide contained in a 500-ml. three-necked flask fitted with a mercury-sealed stirrer and a reflux condenser. Then 6 gm. (0.15 mole) of pul-

verized sodium hydroxide was quickly added, with continuous stirring, and was washed down with 50 ml. more of carbon disulphide. The reaction was exothermic, and a heavy, pale yellow gel formed within 10 min. After the mixture had been kept overnight, 37.4 ml. (0.60 mole) of methyl iodide was added in portions, with stirring, and by the next day the gel had been completely replaced by a pale yellow liquid containing a white precipitate of sodium iodide. After dilution with an equal volume of ether and after filtration, the liquid was evaporated under reduced pressure, finally in a vacuum desiccator. The yellow liquid, 50.2 gm. (100.5%), solidified to a pale yellow solid melting at 24–25° after remaining in a cold room for some time.

The product was twice recrystallized from a large excess of ethanol, each time in three or four crops, the yield of nearly pure white crystals being 40 gm. A third, similar crystallization gave a first crop of 27.2 gm. (54%) with the final melting point of 28–28.5°, and the small sample for analysis was recrystallized once more before being dried over phosphorus pentoxide in an evacuated desiccator kept in the cold room. Found: C, 64.7, 64.6, 64.9; H, 10.6, 10.9, 11.0; S, 20.0, 19.1%. Calc. for $C_{18}H_{36}OS_2$: C, 64.8; H, 10.9; S, 19.3%.

The 250 ml. of carbon disulphide used as the reaction medium could be replaced by a somewhat larger volume of ether.

Crude Sodium Octadecyl Xanthate

Pulverized sodium hydroxide, 3.2 gm. (0.08 mole), dry ether, 280 ml., and pure octadecanol, 21.6 gm. (0.08 mole), were stirred together in a flask equipped as described above. Although the octadecanol failed to dissolve completely, the stirring prevented a solid cake from forming. The thick suspension broke down immediately 9.6 ml. (0.16 mole) of carbon disulphide was added; the solution became yellow and the yellow xanthate salt gradually formed. After six hours of stirring and gentle warming, a further 9.6 ml. of carbon disulphide was added and the mixture was kept overnight. The salt was recovered on a filter and when dried in the air appeared as pale yellow crystals weighing 27.3 gm. (92.6%).

Following the procedure of DeWitt and Roper (10), the salt was dissolved in hot acetone, the solution filtered to remove 2 gm. of insoluble material, and then slowly diluted with benzene to cause reprecipitation. After a second purification, in which petroleum ether replaced benzene as the precipitating agent, the salt, now white, was dried in a vacuum desiccator containing phosphorus pentoxide, activated charcoal, and paraffin wax. Yield, 19.1 gm. (65%). Found: S, 15.4 (hypobromite method), 15.0% (Carius). Although white, the salt gave a very turbid solution in 4% aqueous sodium hydroxide and was obviously impure. An attempt at recrystallization from warm ethanol caused continual decomposition, since the clear solution rapidly became turbid. Finally, the salt was dissolved in an excess of acetone, the solution was filtered and diluted with about 10 volumes of pentane. Next day the white crystals were recovered and dried in a vacuum desiccator. Found: S, 14.8, 15.1 (Carius); Na, 4.74, 5.15% (sulphated ash); "iodine equivalent", 294. Calc. for $C_{19}H_{37}OS_2$-Na: S, 17.4; Na, 6.24%; "iodine equivalent", 344. The iodine equivalent was obtained by titrating a weighed sample of the salt, dissolved in aqueous ace-

tone, with 0.1 *N* iodine, using a small layer of ether or carbon tetrachloride to determine the end point. The results were calculated according to Whitmore and Lieber (26) as milligrams of iodine per gram of xanthate salt. All the analyses showed that the sodium octadecyl xanthate had a purity of only 80 to 87%, but no means of purifying it further could be found.

O-Octadecyl S-Methyl Xanthate

(*a*) Octadecanol, 40.5 gm., was stirred in a flask (equipped as described above) with 250 ml. of carbon disulphide for several hours until solution was complete. When 6 gm. of pulverized sodium hydroxide was added with stirring, the heavy, pale yellow precipitate of the xanthate salt formed almost immediately, and one day later 37 ml. of methyl iodide was added. After the mixture had been gently warmed for a short time, and then allowed to stand for two days, an equal volume of ether was added to bring about a better separation of the sodium iodide.

The filtrate and washings when evaporated under reduced pressure, finally in a desiccator, left 48.1 gm. (89%) of a pale yellow solid melting at 37.5–38°. Recrystallization from 300 ml. of ethanol yielded four crops, of which the first two, 32.1 gm. (60%), melted at 37.5–38.5° and at 36–37°, respectively. The third and fourth crops, 8.6 gm., melting near 53°, were largely octadecanol. A sample of the purest material after three more recrystallizations from ethanol melted at 38–39°. Found: C, 66.5, 66.5; H, 11.0, 11.0; S, 17.9, 17.7%; mol. wt. (Rast), 388, 352. Calc. for $C_{20}H_{40}OS_2$: C, 66.6; H, 11.2; S, 17.8%; mol. wt., 360. The volatility of octadecyl *S*-methyl xanthate in steam, although slight, exceeded that of the parent octadecanol. When a 5 gm. sample of the ester was slowly heated, a thermometer being inserted directly into the pale yellow melt, a vigorous reaction occurred at 180–190° and the temperature increased to about 290°. Only a few drops of distillate were obtained at 315°, and the still residue on cooling separated into nearly equal amounts of a white solid and a pale yellow liquid. Both dissolved in ether, but neither was examined further.

(*b*) The same ester was also obtained in good yield by the action of methyl iodide on the sodium octadecyl xanthate isolated above.

Nitrosomethylurethane and Sodium Octadecyl Xanthate

A clear solution of the crude sodium salt described above, 1 gm. (2.7 mM.), in 100 ml. of absolute methanol was placed in a 500-ml. three-necked flask fitted with a mechanical stirrer, a thermometer, and a dropping funnel. Nitrosomethylurethane, 1.79 gm. (13.5 mM.), dissolved in 20 ml. of absolute methanol, was added dropwise at 3–5° during 20 min. After about five minutes a white foamy solid appeared on the surface of the solution, and increased in amount until the nitrosomethylurethane had all been added. Two hours later, when the temperature had risen to 15°, the solid was separated, was washed with a little absolute methanol, and was dried over phosphorus pentoxide in a vacuum desiccator. Concentration of the filtrate yielded a second crop, and a third was obtained by diluting the final mother liquor, 20 ml., with 250 ml. of water. The first two crops, totalling 0.87 gm. or 89%, melted at 36–38.5°, and

two recrystallizations from ethanol failed to alter this value significantly. A mixed melting point with authentic octadecyl *S*-methyl xanthate was not depressed. Found: S, 17.6, 17.9%. Calc. for $C_{20}H_{40}OS_2$: S, 17.8%.

Alkali and S-Methyl Xanthates

(*a*) *Alcoholic Sodium Hydroxide*

The data were summarized in Table I. In order to recover the white precipitate which persisted throughout the saponification, which in this case was for one hour under reflux, the final mixture was evaporated to dryness. Extraction with boiling ether removed 97% of the calculated amount of octadecanol as a white solid melting at 55–57° and yielding the corresponding phenylurethane with the correct melting point of 79.5° (3). A 5.96 gm. sample of benzyl *S*-methyl xanthate, when boiled for 90 min. with 75 ml. of 1.2 *N* sodium hydroxide in 90% ethanol, yielded 2.16 gm. of redistilled benzyl alcohol (67%) from which a phenylurethane with the correct melting point of 77–78° was prepared.

The recoveries of octadecyl *S*-methyl xanthate, m.p. correct at 37–38°, were about 99% both from boiling 25% aqueous sodium hydroxide and from *N* 95% aqueous alcoholic ammonia at room temperature. Over 75% was recovered by evaporating a solution in pyridine which had stood for one week and by recrystallizing the residue from ether.

(*b*) *Thallous Ethylate*

Octadecyl *S*-methyl xanthate, 0.299 gm. (0.83 mM.), was dissolved at 5–10° in 25 ml. of a 0.095 *N* solution (1.9 mM.) of thallous ethylate in pure, dry benzene. Within a few seconds, the solution became yellow and turbid, and after a few minutes, deep brown. The reaction was perhaps one-third complete in 70 min. After the solution had been kept for 12 hr. in the dark, 50 ml. of 0.099 *N* hydrochloric acid and 20 ml. of methanol were added to decompose the remaining thallous ethylate, and the excess acid was back-titrated to a phenolphthalein end point with standard sodium hydroxide. The consumption of thallous ethylate was 1.63 mM., or 1.99 moles per mole of the xanthate ester.

In another experiment, 0.608 gm. (1 mM.) of *O*-octadecyl *S*-methyl xanthate was kept for 12 hr. in the dark with 50 ml. of the thallous ethylate solution. The mixture was filtered on sintered glass, and the black residue, which evolved hydrogen sulphide when treated with acid, was probably thallium sulphide. The clear, nearly colorless filtrate, which soon became turbid, when evaporated under reduced pressure gave a yellow brown solid. A solution of this solid in ether, when clarified by filtration and evaporated, left 0.64 gm. (106%) of near-white crystals with an unpleasant odor. When recrystallized from pentane, white leaflets melting at 56–57.5° were obtained, and from them a phenylurethane melting at 78–78.5°. The melting points recorded for octadecanol and its phenylurethane were 60° and 79.5° (3) respectively.

Acid and Octadecyl S-Methyl Xanthate

(*a*) *Hydrochloric Acid*

A small sample of the ester was heated under reflux with 0.225 *N* aqueous hydrochloric acid for 20 min. No obvious change occurred, and the concen-

tration of hydrochloric acid was increased to 6 *N*. After three hours under reflux, the ester still floated as an oil on the surface; it was later recovered nearly quantitatively and with the correct melting point.

The xanthate ester, 0.300 gm., was then shaken with 25 ml. of ice-cold, concentrated hydrochloric acid (43.3%), but failed to react or dissolve within 24 hr. at 0°. The mixture was then diluted with an equal volume of water and extracted three times with ether to recover 0.308 gm. of a solid residue. Recrystallization from ethanol yielded 0.235 gm. (79%) of the pure *S*-methyl xanthate.

With cooling, 2 ml. of 12 *N* hydrochloric acid was diluted to 24 ml. with ethanol, and 15 ml. of the mixture was boiled under reflux for one hour with a small sample of the *S*-methyl xanthate. Although the latter dissolved, no odor of mercaptan was noticed. The mixture was evaporated, and after being filtered an ethereal extract of the residue yielded 97% of the starting material in a slightly impure state. Recrystallization gave the pure ester.

(*b*) *Methanolic Hydrogen Chloride (3.2%)*

O-Octadecyl *S*-methyl xanthate, 0.31 gm., was warmed under gentle reflux with 50 ml. of the acid reagent, an amount just sufficient to dissolve the ester. The top of the condenser was protected with a calcium chloride guard tube. After 30 min., a trace of methyl mercaptan could be detected by the yellow coloration imparted to lead acetate paper. This decomposition was exceedingly slow, because the product isolated after 72 hr. represented 93% of the original ester and had the correct melting point. The experiment was repeated using a sealed glass tube, which was kept at 120° for three days before being cooled and opened. The solution suddenly evolved much gas, which caused a mechanical loss of the product. The remaining product, 39%, was the original ester.

In another experiment, 0.2 gm. of the ester and 10 ml. of the methanolic hydrogen chloride were kept at 125° for three days, as before, but the tube and its colorless contents were further heated to 140° for two days, and then at 160° for 33 hr. Once more a violent evolution of gas destroyed the quantitative aspect of the recovery, but the product after recrystallization from pentane had the melting point, 59–60°, of octadecyl alcohol.

(*c*) *Acetic Anhydride – Zinc Chloride*

A small test tube containing the *S*-methyl xanthate, 0.5 gm., acetic anhydride, 2.5 gm., and anhydrous zinc chloride, 0.025 gm., was stoppered, shaken thoroughly, and kept at room temperature for 24 hr. When the mixture was poured onto ice, no solid appeared other than the original ester, which had never dissolved. Yield, 96.7%, with melting point correct at 37.5–38.5°.

Desulphurization of Octadecyl S-Methyl Xanthate

The pyrophoric Raney nickel "W-2" catalyst (19) was washed quite free of alkali and was stored under absolute ethanol. About 45 gm. of this catalyst, weighed wet with ethanol, was mixed with 7.2 gm. of octadecyl *S*-methyl

xanthate and enough absolute ethanol to increase the volume to 150 ml. The mixture was boiled for four hours under reflux, and for at least an hour of this period a substance which turned lead acetate paper bright yellow and which had an unpleasant odor (not that of hydrogen sulphide) was evolved from the condenser. After being recovered by filtration through sintered glass, the residual nickel, still pyrophoric, was washed with warm ethanol, but still appeared to retain some of the product.

The filtrate and washings, from which a white solid tended to separate, were evaporated, and the residue was freed from traces of nickel by solution in ether and by filtration. After recovery from the ether the product, 5.4 gm., was fractionally recrystallized from pentane, absorbent carbon being used for clarification. The first two crops, totalling 2.2 gm. (40%), were shown by recrystallization to a melting point of 58–59° to be essentially octadecanol. Evaporation of the original mother liquors gave 1.97 gm. of a solid residue melting at 28.5–30°.

This residue when fractionated from methanol–ether yielded three crops of white ill-formed crystals; 0.742 gm., m.p. 28–30°; 0.333 gm., m.p. 28–30.5°; and 0.114 gm., m.p. 28–30.5°. The first fraction when recrystallized from methanol–ether melted at 29.5–31.5°. Found: OCH_3, 2.6, 2.6%. A combination of similar white, waxy residues from several experiments was then "recrystallized" twice from methanol without changing the melting point. Found: S (Carius), 2.1, 2.4, 2.3%. The product gave no green color with isatin in the test for a mercaptan (7), and did not dissolve in boiling 5% sodium hydroxide. A sodium hydroxide fusion test for oxidized sulphur (7), which depended on the change in color of nickelous hydroxide caused by sulphur dioxide, was no more positive than a blank. Although the substance was probably a mixture, it might have contained octadecyl methyl ether (calc. OCH_3, 10.9%).

In another experiment, in which 3.6 gm. of *O*-octadecyl *S*-methyl xanthate was treated with Raney nickel for only 10 min. near 10°, the low-melting residue from the crystallization of octadecanol weighed 1.35 gm. and melted at 27–28°. When fractionally recrystallized, the head fractions yielded 0.487 gm. of the original *S*-methyl xanthate with the correct melting point of 37°, which liberated mercaptan when heated with alcoholic sodium hydroxide.

Oxidations with Hydrogen Peroxide and Periodic Acid

(*a*) *O-Octadecyl S-Methyl Xanthate*

Seven grams (0.019 mole) of the xanthate ester was dissolved in 900 ml. of glacial acetic acid, an amount necessary to prevent precipitation of the ester when 11.3 ml. of 30% hydrogen peroxide (0.117 mole) was added with thorough mixing. About 90 min. later the clear solution began to deposit a white solid. After three days at room temperature, the liquor was diluted with an equal volume of water, the mixture was chilled, and the white, waxy precipitate isolated by a difficult filtration. Yield, 6.1 gm.; m.p., 49–52.5°. This product, when fractionally recrystallized, once from ethanol and twice from pentane, yielded 2.24 gm. (33.5%) of white flakes whose melting point

of 66–67° was not significantly changed by four more recrystallizations. Found: C, 58.6, 58.6; H, 10.1, 9.8; S, 15.5, 15.7, 15.6%; mol. wt. (Rast), 395, 420, 420, 426. Calc. for $C_{20}H_{40}O_4S_2$: C, 58.8; H, 9.9; S, 15.7%; mol. wt., 408.

The sodium hydroxide fusion test for oxidized sulphur (7) was no more positive than a blank, and another sample of the crystals was recovered with unchanged melting point after being boiled for 10 min. with concentrated hydrochloric acid. A third portion, when warmed briefly with 5% sodium hydroxide, melted, but resolidified to a white wax when the mixture cooled. In an attempt to saponify the compound, 1 gm. was heated under reflux with 30 ml. of 25% sodium hydroxide for seven hours, when no further change was apparent. The solid first melted, then partly solidified; finally the solution was yellow, and the substance floating on the surface had again liquefied. A steam distillation of the mixture produced a condensate containing a slightly volatile wax melting at 59.5–61.5°. This melting point, together with that of 79° found for the phenylurethane, identified the wax as octadecanol. The residue in the still gave a clear filtrate which liberated hydrogen sulphide when acidified and which produced a heavy black precipitate with a solution of lead acetate. Therefore at least one sulphur atom in the compound $C_{20}H_{40}O_4S_2$ was still in the reduced state. The acidified filtrate contained no sulphate ion, according to a test with barium chloride.

(*b*) *O-Hexadecyl S-Methyl Xanthate*

Following the procedure described for the octadecyl derivative, a solution of 13.3 gm. (0.04 mole) of the pure *O*-hexadecyl *S*-methyl xanthate in 1800 ml. of glacial acid was mixed with 0.24 mole of aqueous hydrogen peroxide. It was nearly a day before a precipitate began to form, and the product was isolated after three days. Yield, 8.5 gm. (56%); m.p., 42–44°. One recrystallization from ethanol and four from pentane raised this melting point to a constant value of 56–57°. Found: C, 57.0, 56.9; H, 9.6, 9.7; S (Waters), 17.0, 16.7%. Calc. for $C_{18}H_{36}O_4S_2$: C, 56.8; H, 9.5; S, 16.9%.

(*c*) *Paraperiodic Acid, H_5IO_6*

Octadecyl *S*-methyl xanthate was too insoluble to react with sodium periodate in water, and the reaction in 85% aqueous dioxane was very slow. In the final experiment, a solution of 1.9 gm. (8.3 mM.) of crystalline paraperiodic acid in 40 ml. of ethanol was mixed in a stoppered flask with 1 gm. (2.8 mM.) of the *S*-methyl ester in 100 ml. of ethanol. A deep red color soon developed in the solution, which after a week was diluted with 750 ml. of water. The silk-like precipitate containing iodine crystals was recovered, and the latter were allowed to evaporate in the open air. The remaining 0.339 gm. was recrystallized twice from ethanol–water to give a white wax melting at 33–34°.

Attempted Estimations of the Methylthio Group

(*a*) *With Hydriodic Acid*

The acid used boiled constantly at 127°, and good checks were obtained when the methoxyl content of vanillin (OCH_3, 20.4%) was determined both by the Kirpal–Bühn (13) and the Vieböck (23) methods.

Found by the Vieböck method, with heating for 90 min.: SCH_3, 0.13, 1.15%; with heating for 150 min.: SCH_3, 0.51, 0.63%. Found by the Kirpal–Bühn method, with heating for five hours: SCH_3, 2.14, 2.42%. Calc. for *O*-octadecyl *S*-methyl xanthate, $C_{20}H_{40}OS_2$: SCH_3, 13.1%.

Found by the Vieböck method, with heating for one hour: SCH_3, 1.35, 2.34%. Found by the Kirpal-Bühn method, heating for four hours: SCH_3, 2.7, 1.9%. Calc. for benzyl *S*-methyl xanthate, $C_9H_{10}OS_2$: SCH_3, 23.7%.

(*b*) *With Bromine*

The method described by Siggia and Edsberg (22) for estimating thio ethers by oxidation to sulphoxides was modified. Weighed samples of pure *O*-octadecyl *S*-methyl xanthate were dissolved with difficulty in glacial acetic acid, a little hydrochloric acid was added, and the mixtures were titrated with 0.1 *N* potassium bromate – potassium bromide to a yellow end point. The end points were very indistinct, but corresponded roughly to the oxidation of both sulphur atoms in the xanthate ester. Attempts to keep the ester in solution by warming the acetic acid, or by replacing it with ethanol, gave still higher and still less reliable results. The ester reduced about 11 equivalents of bromine per mole.

In order to isolate the product, 8 gm. (0.022 mole) of the ester was dissolved in 600 ml. of warm ethanol and 50 ml. of water. This solution readily decolorized 7 ml. (about 13 equivalents) of bromine, a further 5 ml. being utilized within 16 hr. The orange liquid was then warmed to expel excess bromine and to redissolve a precipitate that had formed; 1.5 vol. of warm water was added, and a white wax, instead of an oil, separated provided that the solution cooled slowly to 10°. Yield, 6.3 gm. Three recrystallizations from pentane and two from ethanol rendered the melting point constant at 61.5–62.5°. This product gave negative tests for sulphur and halogens, did not dissolve in 5% sodium hydroxide, but turned bright yellow in color. A test for aldehyde group with dinitrophenylhydrazine was negative.

ACKNOWLEDGMENT

One of us (D. L. V.) wishes to thank the Spruce Falls Power and Paper Company, Limited, and the American Viscose Corporation for the Fellowships he enjoyed during the research; also the Pulp and Paper Research Institute of Canada for summer stipends.

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THE CHEMISTRY OF LYCOCTONINE[1]

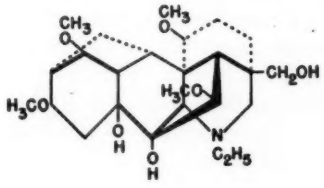
By O. E. Edwards, Léo Marion, and D. K. R. Stewart[2]

ABSTRACT

New observations in the chemistry of hydroxylycoctonine and other derivatives of lycoctonine, and the previously described reactions of the alkaloid, are interpreted using the structure as recently determined by X-ray crystallography.

During the last few years we have explored the chemistry of lycoctonine, and have proposed partial structures to account for the observed facts (3, 4, 5, 6). The determination in these laboratories of a total structure for des(oxymethylene)-lycoctonine using X-ray crystallography (11) makes it desirable to discuss these facts and further observations in the light of this formulation.

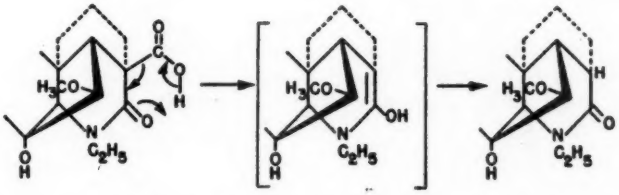
The proposed structure for des(oxymethylene)-lycoctonine leads without ambiguity to formula I or its mirror image for lycoctonine. The location of the



I

CH_2OH at the bridgehead of an azabicyclo[3,3,1]nonane system corresponds satisfactorily with the relatively unhindered nature of the carboxylic acid derived from it by oxidation of the primary hydroxyl and the methylene next to the nitrogen (lycoctonamic acid) (3). Roberts and Moreland (12) showed that esters of a similar acid in the bicyclo[2,2,2]octane series are readily hydrolyzed in contrast to acyclic tertiarily-bound carboxylic acids.

The transition state for the decarboxylation of lycoctonamic acid and the transient enolic intermediate would involve a bridgehead double bond as shown:

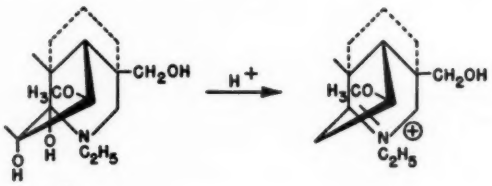


However, the work of Meerwein (9) has demonstrated that Bredt's rule can be violated to the extent of formation of such transient intermediates in the

[1]*Manuscript received April 20, 1956.*
Contribution from the Division of Pure Chemistry, National Research Council, Ottawa, Canada. Issued as N.R.C. No. 4041.
[2]*National Research Council Postdoctorate Fellow, 1955–56.*

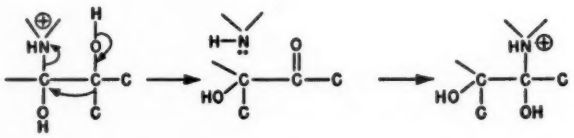
bicyclo[3,3,1]nonane system (see Reference 7 for an excellent review of Bredt's rule).

We have confirmed the observation of Cookson and Trevett (2) that hydroxylycoctonine (II) forms anhydronium salts (III). This is not too readily reconciled with the new structure, since the double bond demanded by this formation introduces marked strain.

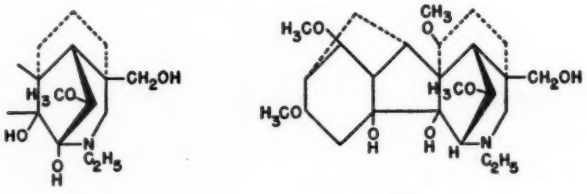


II III

If structure I is correct, then isolycoctonine, which is obtained by reduction of hydroxylycoctonine (II) in ethanolic-hydrochloric acid in the presence of Adams' catalyst (3), cannot be a simple epimer at the carbon next to the nitrogen as we had assumed. Hence it must be a rearrangement product. The simplest possibility seems to be that hydroxylycoctonine (II) is in equilibrium with the alternate masked α-ketol (IV) via the open ketone as shown:



If, now, IV is much more rapidly reducible than II as a result of the more exposed nature of the carbinolamine carbon, the production of V as the main product is understandable. We thus consider it probable that V is the structure of isolycoctonine. That the open ketone is present in acid solution is indicated

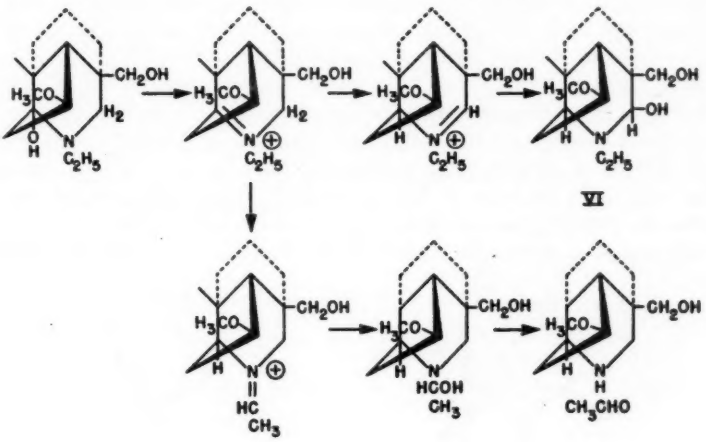


IV V

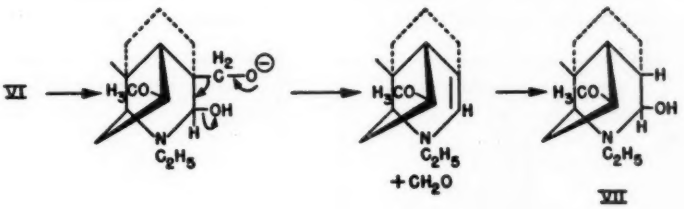
by the presence in ethanol solutions of hydroxylycoctonine salts and of hydroxylycoctonine in glacial acetic acid of a maximum at 320 mμ, ϵ 70. No such band is present in the solution of the anhydronium salts of atisine, isoatisine, and 17-hydroxylupanine.

Hydroxylycoctonine was only slowly attacked by lithium aluminum hydride in refluxing dioxane. Sodium borohydride in aqueous alcohol gave a mixture of bases which was not further investigated.

The environment of the nitrogen readily accounts for the products obtained when an aqueous solution of hydroxylycoctonine was heated. The products identified were lycoctonine, des(oxymethylene)-lycoctonine, formaldehyde, and acetaldehyde. These can arise as shown using the partial formulae:



The carbinolamine VI can readily lose formaldehyde as shown:



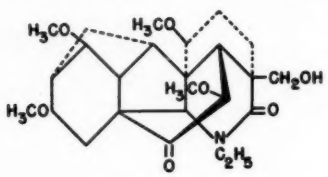
VI and VII are then reduced, presumably by the formaldehyde and some of the carbinolamine present, in crossed Cannizaro reactions to lycoctonine and des(oxymethylene)-lycoctonine respectively. A likely mechanism for reduction by formaldehyde is illustrated:

The facile loss of formaldehyde from VI provides an explanation of the formation of des(oxymethylene)-lycoctonam during permanganate oxidation

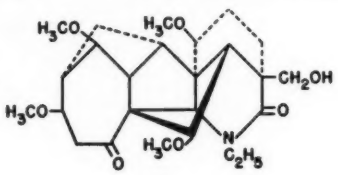
of lycoctonine. Thus VI must be formed as the first product of oxidation and have sufficient resistance to further oxidation that some has time to eliminate formaldehyde before the lactam is formed. That carbinolamines are intermediates in the permanganate oxidation of amines is also demonstrated by the formation of acetaldehyde from the $N—C_2H_5$ group of the aconite alkaloids (3).

It is evident that most of the chemistry of the heterocyclic ring is understandable on the basis of the new formula. However, one published fact which is in apparent conflict with the structure is the striking increase in resistance to hydrolysis of methyl hydroxylycoctonamate over methyl lycoctonamate (5), since the new hydroxyl and the carboxyl group are remote in space.

The geometry of the proposed structure demands that the pinacolic dehydration of the vicinal glycol in lycoctonam take one of two courses to give VIII or IX. Since IX should readily lose methanol to give an α-β unsaturated ketone with acid or base, it can be excluded from consideration since the anhydro compounds are relatively stable to these agents. Hence VIII must be the skeleton of anhydrolycoctonam (3, 6). The failure of anhydrolycoctonam



VIII



IX

to give readily a positive Fehlings and Tollens test was hence misleading as to the direction of the migration during the dehydration (6).

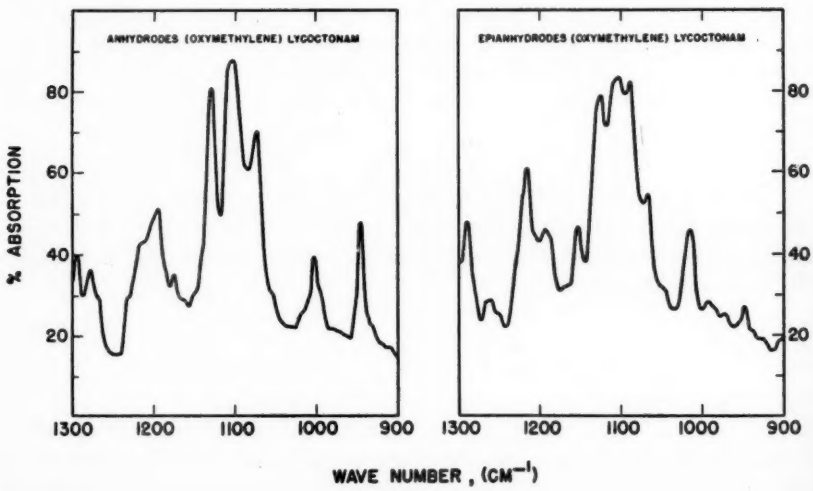
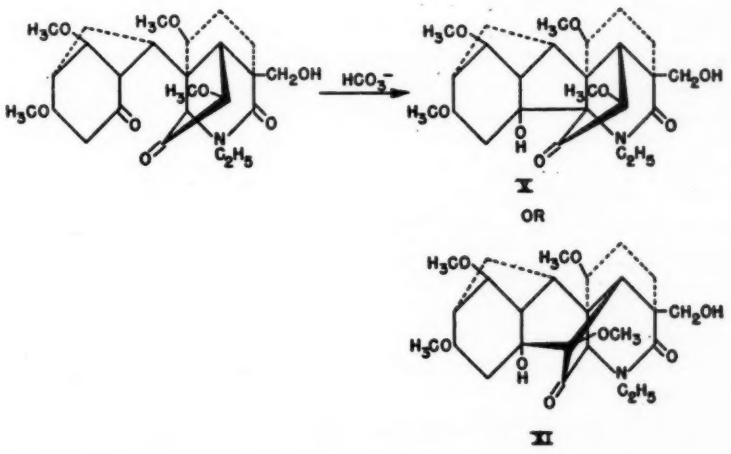


FIG. 1

The interesting observation that, whereas anhydrolycoctonam (VIII) is stable to hot dilute alkali, anhydrodes(oxymethylene)-lycoctonam is transformed into an isomer is in harmony with the assigned structure. The reaction of anhydrodes(oxymethylene)-lycoctonam must be epimerization at the carbon α to the ketone carbonyl. This is borne out by the fact that the infrared spectrum of the product differs very little from that of the starting material, except for the disappearance of one methoxyl band at 1073 cm.$^{-1}$ and appearance of a new band at 1079 cm.$^{-1}$ (Fig. 1).

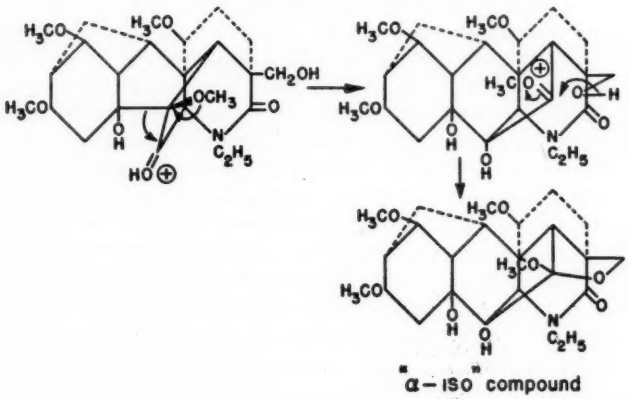
The replacement of the CH_2OH by hydrogen makes the epimer with the methoxyl directed toward this hydrogen the most stable one while the converse is true as long as the bulky CH_2OH is present (VIII).

Most of the reactions of the secodiketones derived by periodate cleavage of the vicinal glycol are readily accounted for using the new formula. The "iso" compounds derived from the secodiketones by adsorption on weakly acidic alumina or by treatment with sodium bicarbonate (4) must be the internal aldol condensation product XI:



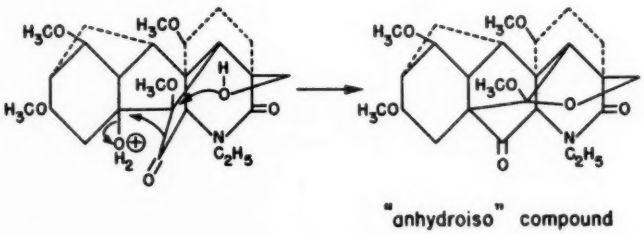
The methoxyl at the point of condensation may be epimerized during the preparation of the secodiketones, or during the condensation, to give XI. The structure X is unlikely since the enolization of the ketone in the requisite direction for its formation would place a bridgehead double bond in the small branch of an azabicyclo[3,2,1]octane system in serious violation of Bredt's rule.

The action of hot dilute acid on the "iso" compound gave rise to a mixture from which two crystalline products (called the "α-iso" and "anhydroiso" compounds) were obtained (4). The "α-iso" compound, which was isomeric with the "iso" compound, but had lost the ketonic function and the primary hydroxyl while gaining a new hindered hydroxyl, we consider to arise from XI as shown:



It is intriguing that in this structure the lycoctonine skeleton, including the vicinal glycol, has been re-formed. Experiments are underway to test this hypothesis.

The "anhydroiso" compound, which from analyses and spectra seemed to be the product of ether formation between the primary and tertiary hydroxyl, can be explained by postulating an acyl migration (probably a two step process as for the "α-iso" compound):



House and Reif (8) and Meinwald (10) have discussed similar migrations. The geometry is good for the migration, and the final structure, while somewhat crowded, is not particularly strained. The position of the carbonyl absorption in the infrared for the "anhydroiso" compound (1736 cm.$^{-1}$) is high for the suggested six-membered character. (The somewhat comparable carbonyl in the anhydrolycoctonam types, however, absorbs as high as 1740 cm.$^{-1}$.)

The survival of the ketals in the hot acid, if the above postulates are correct, calls for comment. The double bond in the oxonium ion intermediate in the most probable hydrolysis pathway does not appear unduly strained in models. However, the moderate strain in this intermediate, the competitive protonation of the ring oxygen (which probably would not lead to hydrolysis), and protonation of the more basic lactam may all combine to make hydrolysis of the ketal a slow process.

The failure of hydroxylycoctonine to consume more than 1 mole of HIO_4 led us to the conclusion that there was no vicinal triol system in the compound. Since the new formula demands the presence of such a triol, the cleavage was tested further. Hydroxylycoctonine reacts with 1 mole of $Pb(OAc)_4$ in 48 hr. in dilute acetic acid solution, but the reagent is taken up steadily beyond this until after 528 hr. 3.5 moles have been consumed. Hydroxylycoctonam on the other hand rapidly takes up 1 mole of $Pb(OAc)_4$ but the oxidation then stops. After 315 hr. only 1.26 moles is taken up, no more than is consumed by lycoctonam itself. That the oxidation cleaves the original vicinal glycol is demonstrated by the infrared spectrum of the resulting diketone which has carbonyl bands at the same frequency as *seco*lycoctonam diketone, and the formation of a desmethanol derivative during the oxidation or subsequent chromatography with infrared and ultraviolet spectra again very similar to desmethanol-*seco*lycoctonam diketone. Hydroxy*seco*lycoctonam diketone monoacetate is resistant to permanganate oxidation in acetone, and inert to sodium bismuthate in acetic acid at room temperature. Only a small quantity of acidic material was produced when desmethanolhydroxy*seco*-lycoctonam diketone was treated at 0° with alkaline hydrogen peroxide. Thus we have been unable to provide direct evidence for the presence of a vicinal triol in hydroxylycoctonam.

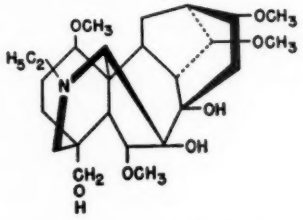
A third neutral compound which was strongly adsorbed on alumina was isolated from among the lead tetraacetate cleavage products. It appears to have the empirical formula $C_{24}H_{35}NO_9$. Since it was not readily acetylated it probably has no primary hydroxyl while the spectra indicate the presence of two ketone carbonyls, at least one hydroxyl, and the lactam. The properties are consistent with a structure in which the CH_2OH of the *seco* diketone has been replaced by OH.

The work reported in this paper clearly shows the difficulty of demonstrating two of the vital points needed in determining the structure of lycoctonine by chemical means: whether or not hydroxylycoctonine has the same skeleton as lycoctonine, and the relation between the heterocyclic ring and vicinal glycol. The difficulties encountered in attempts to determine the degree of substitution of the carbon holding the hydroxymethylene group will be described in a later paper. Thus it appears that the solution of the structural problem by ordinary degradative methods would have been extremely difficult.

Finally, it must be pointed out that the suggestions advanced in an earlier paper (6) for the course of the acid-catalyzed transformation of anhydro-lycoctonam into lycoctamone are untenable and the structure of lycoctamone is as yet unsettled. One possible formulation of this interesting product is currently being tested experimentally.

While the chemistry of delpheline (1) is readily interpreted using the same carbon skeleton as that of lycoctonine, the reactions of delphinine, in particular the two-stage Hofmann degradation (13) and the Grignard reactions of oxodelphinine (14), seem to demand a different sort of structure for this alkaloid.

The structure of lycoctonine can be projected in such a way as to emphasize its diterpenoid character*:



Since atisine, the only other aconite alkaloid about which much is known, almost certainly has a diterpenoid carbon skeleton also, it seems likely that all delphinium and aconite alkaloids will be found to have structures derived from various modified diterpenoid skeletons.

EXPERIMENTAL

Rotations were determined in absolute ethanol, the cited temperature being that of the room. The ultraviolet spectra were determined on solutions in 95% ethanol using a Beckmann D.U. spectrophotometer. Infrared spectra were determined on a Perkin-Elmer model 21 double beam spectrophotometer.

Hydroxylycoctonine

When prepared by oxidation of lycoctonine with a mole of $Pb(OAc)_4$ in acetic acid (2) the compound was obtained in 75% yield. It readily crystallized from concentrated acetone solution as rectangular plates. Its physical constants were very close to those described earlier (3): m.p. 148–152°, $[\alpha]_D$ $+13°\pm1°$ (*c*, 2.0 in ethanol). Its infrared spectrum (nujol mull) had no bands between 1500 and 2800 $cm.^{-1}$.

The hydriodide of the base, m.p. 198° dec., when reanalyzed gave figures in good agreement with theory for an anhydronium salt. Found: C, 50.51, 50.94; H, 6.70, 6.82. Calc. for $C_{25}H_{42}NIO_7$: C, 50.58; H, 6.79. The infrared spectrum of the salt (nujol mull) contained bands at 1670 and 1712 $cm.^{-1}$ as described by Cookson and Trevett (2). The relative intensity of these bands was unaffected by the mode of preparation of the salt, or by heating it dry or in methanol solution. Its ultraviolet absorption spectrum had strong featureless absorption at short wavelengths (log ϵ 3.39 at 240 mμ and 3.04 at 250 mμ) and λ_{min} 305 mμ (log ϵ 1.72), λ_{max} 330 mμ (log ϵ 1.85). The absorption spectrum of a solution of hydroxylycoctonine in acetic acid had λ_{max} 330 mμ (log ϵ 1.85).

*We are indebted to Dr. R. C. Cookson who pointed out this fact in a private communication.

Reduction of Hydroxylycoctonine

Approximately 350 mgm. of lithium aluminum hydride in 25 ml. of ether was added to a solution of 300 mgm. of hydroxylycoctonine in 15 ml. of dioxane. The ether was boiled off and the dioxane solution refluxed under nitrogen for two hours. The excess reagent was decomposed with ethyl acetate, the dioxane removed *in vacuo*, 15 ml. of saturated Rochelle salt solution added, and the base extracted into methylene chloride. The extract gave 280 mgm. of methanol-soluble base. This crystallized from concentrated aqueous methanol, giving 170 mgm., m.p. 149–152°, which did not depress the melting point of hydroxylycoctonine. The remaining base would not crystallize.

A solution of 100 mgm. of hydroxylycoctonine in 2 cc. of 50% aqueous methanol containing 89 mgm. of sodium borohydride was left at room temperature for 18 hr. A concentrated aqueous solution of the 83 mgm. of base recovered from the reaction deposited 20 mgm. of crystals, m.p. 156–161°. The mother liquors were acidified, warmed for five minutes, then left at room temperature for two hours. The 65 mgm. of base recovered from this solution slowly crystallized from water on addition of ammonia, giving 32 mgm. of tiny plates, m.p. 128–134°. When recrystallized from acetone this gave rectangular plates, m.p. 132–140°. Mixed m.p. with hydroxylycoctonine 137–145°. The base in the mother liquors remained amorphous.

Action of $Pb(OAc)_4$ on Hydroxylycoctonine

A solution was prepared of 76 mgm. of hydroxylycoctonine in 15 cc. of a 0.056 molar solution of lead tetraacetate in acetic acid. At intervals an aliquot was removed, added to a solution of potassium iodide in saturated sodium acetate containing a known excess of sodium thiosulphate solution, and the excess back-titrated with iodine. The mole ratio of lead tetraacetate consumed was 0.60 (24 hr.); 1.08 (48 hr.); 1.79 (96 hr.); 2.35 (166 hr.); 2.74 (239 hr.); 3.22 (382 hr.); 3.5 (528 hr.).

Action of Hot Alkali on Hydroxylycoctonine

A solution of 40 mgm. of hydroxylycoctonine in 5 cc. of methanol containing 240 mgm. of potassium hydroxide was refluxed for six hours, then left overnight at room temperature. The recovered base (40 mgm.) gave 18 mgm. of starting material, m.p. 148° (mixed m.p. 149°). The residual base or its hydriodide could not be obtained crystalline. This residue had $[\alpha]_D$ −12° (*c*, 1.6 in ethanol), hence a new base or bases had been formed.

Heating of Hydroxylycoctonine in Water and Aqueous Alcohol

(*a*) 333 mgm. of pure hydroxylycoctonine in 6 cc. of 20% ethanol in water was heated at full steam bath temperature for eight hours, then left overnight at room temperature. The solution was taken to near dryness under reduced pressure. The residue when diluted with water deposited 135 mgm. of fine needles, m.p. 110–115°, $[\alpha]_D$ +44° (*c*, 1.88 in EtOH), which when mixed with lycoctonine melted at 117–130° dec. The mother liquor was acidified and extracted with methylene chloride, the organic phase yielding 8 mgm. of

amorphous neutral material. The acid solution on basification and extraction with methylene chloride gave 150 mgm. of amorphous base with $[\alpha]_D$ +41° (*c*, 3.0 in ethanol).

The amorphous base was combined with 28 mgm. of similar base from a previous run, and converted to its hydriodide. A solution of this deposited 29 mgm. of hydriodide, m.p. 194° dec. (infrared spectrum identical with that of lycoctonine hydriodide). The mother liquor on addition of ether gave 88 mgm. of crystals, m.p. 150° dec., which proved to be impure des(oxymethylene)-lycoctonine hydriodide (see below).

Formaldehyde Characterization

(*b*) Hydroxylycoctonine (55 mgm.), 45 mgm. of dimedon, and 34 mgm. of anhydrous sodium carbonate in 3 cc. of water gave a clear solution when heated, which had a pH near eight. This was heated on the steam bath under a condenser for four hours. The solution was cooled and neutralized with dilute sulphuric acid. The 21 mgm. of precipitate that formed, when recrystallized from methanol, separated as needles, m.p. 192–193°. A mixture with authentic dimedon–formaldehyde derivative (193–194°) melted at 192–193.5°.

(*c*) A solution of 151 mgm. of hydroxylycoctonine in 5 cc. water was heated for four hours on the steam bath, cooled, and the solution filtered. Forty-one milligrams of lycoctonine, m.p. 118–126°, was obtained. A few drops of the filtrate was added to 5 cc. of chromotropic acid in 50% sulphuric acid. A purple color appeared after a few minutes' heating at 100°, and increased steadily in intensity. The solution after 0.5 hr. had the intense maximum ($E_{1\ cm.}$ = 1.05) at 570 mμ characteristic of the condensation product with formaldehyde. Hydroxylycoctonine alone (2 mgm. in 8 ml. of reagent) slowly developed a purple color at 100°, which after 0.5 hr. was still weak ($E_{1\ cm.}$ = 0.12).

Acetaldehyde

(*d*) 244 mgm. of hydroxylycoctonine and 76 mgm. of anhydrous sodium carbonate in 7 cc. of water was heated on the steam bath for 3.5 hr. while nitrogen was bubbled through. The nitrogen was passed through a solution of *p*-nitrophenylhydrazine in dilute acetic acid. After 0.5 hr. a crystalline hydrazone began to separate. At the end of the reaction period 11 mgm. of a *p*-nitrophenylhydrazone had formed, m.p. 124–128°. After two recrystallizations from aqueous methanol the derivative was obtained as fine needles, m.p. 125–129°. Its mixed melting point with acetaldehyde *p*-nitrophenylhydrazone (129–131°) was 126–129°. The main reaction mixture deposited 41 mgm. of needles, m.p. 115–120°. After one recrystallization this melted at 120–127° and did not depress the melting point of lycoctonine. The aqueous mother liquor contained 66 mgm. of neutral product and 94 mgm. of bases. The latter when converted to hydriodide gave 32 mgm. of lycoctonine hydriodide, m.p. 193° dec. (infrared comparison).

Des(oxymethylene)-lycoctonine

Approximately 140 mgm. of the more soluble non-crystalline products from runs similar to (*c*) when separated gave 125 mgm. of bases and 11 mgm. of

neutral products. The bases were converted to hydriodide and crystallized from acetone. A first crop of 20 mgm. of lycoctonine hydriodide was followed by two crops totaling 89 mgm. melting at 175° (dec.). After two recrystallizations this salt melted at 176–177° dec. It did not depress the melting point of des(oxymethylene)–lycoctonine hydriodide monohydrate and the infrared spectra of the two were identical.

Epimerization of Anhydrodes(oxymethylene)-lycoctonam

(*a*) A solution of 35 mgm. of anhydrodes(oxymethylene)-lycoctonam (3) in 5 cc. of 50% aqueous methanol containing 160 mgm. of potassium hydroxide was refluxed for three hours. The 34 mgm. of neutral product crystallized nearly quantitatively as short stout needles from ether. After two recrystallizations 15 mgm. was obtained, m.p. 148–151°, $[\alpha]_D$ +18°±2° (*c*, 0.60). Its infrared spectrum was similar to that of the starting material but contained bands attributable to the epimer.

(*b*) A solution of 116 mgm. of anhydrodes(oxymethylene)-lycoctonam ($[\alpha]_D^{23}$ −8°±1° (*c*, 1.8)) in a mixture of 2 cc. of methanol and 3 cc. of water containing 300 mgm. of potassium hydroxide was refluxed for six hours. The clear yellow solution was concentrated to half volume under reduced pressure, then the product extracted into methylene chloride. The 115 mgm. of pale pink froth crystallized readily from solution in ether. Crop 1, 57 mgm., m.p. 175–190° (hot stage). Crop 2, m.p. 165–175°. Crop 1 when recrystallized from acetone–ether gave a first crop of rhombic plates, m.p. 180–185°, $[\alpha]_D^{23}$ +27° (*c*, 1.95).

Several similar lots of high melting material were recrystallized twice from ethyl acetate – ether, giving prisms showing faint signs of melting at 180° and completely melted by 190° (hot stage), $[\alpha]_D^{22}$ +33° (*c*, 1.45). Its infrared spectrum (mull) had a carbonyl band at 1740 $cm.^{-1}$. Part of the "fingerprint" region is shown in Fig. 1. Found: C, 66.30; H, 8.26; OCH_3, 28.58. Calc. for $C_{24}H_{35}O_6N$: C, 66.50; H, 8.14; $4OCH_3$, 28.63.

Oxidation of Lycoctonam

A 1.00×10^{-2} molar solution of lycoctonam in a saturated solution of lead tetraacetate in glacial acetic acid consumed 1.02 moles of reagent in 2 hr., 1.11 moles in 50 hr., and 1.44 moles in 187 hr.

Oxidation of Hydroxylycoctonam

Hydroxylycoctonam, m.p. 205–208°, (Found: C, 60.16; H, 7.75. Calc. for $C_{25}H_{39}NO_9$: C, 60.34; H, 7.90) (5), was dissolved in a saturated solution of lead tetraacetate to give a 1.00×10^{-2} molar solution. The compound consumed the following mole ratios of reagent: 0.94 (2 hr.), 0.98 (5 hr.), 1.05 (26 hr.), 1.18 (119 hr.), 1.26 (315 hr.). The rate of oxidation did not change when the solvent was 5% and 30% water in acetic acid.

A solution of 3.07 gm. of hydroxylycoctonam in 600 ml. of a saturated solution of lead tetraacetate in acetic acid was left for two hours at room temperature. Saturated sodium sulphite solution was added to reduce excess reagent and the solvent removed under reduced pressure. The residue was taken up in water and the lead salts removed by filtration. The filtrate was

acidified with dilute sulphuric acid and extracted with methylene chloride. The methylene chloride after washing with sodium bicarbonate solution yielded 2.39 gm. of white foam.

The product was adsorbed from benzene onto 96 gm. of neutral alumina, activity 4. A summary of the chromatogram follows:

Eluant	Weight eluted, mgm.
(*a*) Benzene (300 cc.)	125
(*b*) 25% chloroform in benzene (900 cc.)	2124
(*c*) 1% methanol in chloroform (200 cc.)	532
(*d*) 1% methanol in chloroform (100 cc.)	334
(*e*) 50% methanol in chloroform (100 cc.)	128

None of the fractions would crystallize, hence they were acetylated at room temperature with acetic anhydride – pyridine. Group (*a*) yielded 40 mgm. of pure des(oxymethylene)hydroxy*seco*lycoctonam diketone monoacetate and some less pure material. Group (*b*) gave first crops totaling 919 mgm., mainly hydroxy*seco*lycoctonam diketone monoacetate. The first fractions, however, appeared contaminated with the des(oxymethylene) compound ($[\alpha]_D$ −42°) and the last fractions with the strongly adsorbed third compound ($[\alpha]_D$ −38°). From fractions (*d*) and (*e*) was obtained 278 mgm. of the third compound.

Hydroxysecolycoctonam Diketone Monoacetate

The compound crystallized from acetone on addition of ether, m.p. 203–206°, $[\alpha]_D$ −33° (*c*, 1.25). Found: C, 60.45; H, 7.21; OCH_3, 23.16; acetyl, 8.15. Calc. for $C_{27}H_{39}NO_{10}$: C, 60.32; H, 7.31; $4OCH_3$, 23.1; acetyl, 7.81. Its ultraviolet spectrum had a shoulder centering around 280 mμ (log ε 1.91); log ε at 220 mμ was 3.16.

Infrared spectrum (51 mgm. 1 ml. in chloroform, 0.1 mm. cell): 3010(39), 2960(38), 2840(25), 1750(83), 1710(57), 1666(72), 1465(38), 1375(49), 1210–40(74), 1100(77), 1047(58), 990(41), 955(43).

Sodium Bismuthate on the seco Diketone

Hydroxy*seco*lycoctonam diketone acetate (59 mgm.) was dissolved in 5 ml. of acetic acid. Several milligrams of sodium bismuthate was added. No reduction of the bismuthate was evident after three hours at room temperature. After addition of the balance of 1 molar equivalent of $NaBiO_3$ (31 mgm.) the mixture was left for 16 hr. No apparent oxidation of the compound had taken place, hence the reaction mixture was heated at 80°. In 20 min. the color of the Bi_2O_5 was gone. The acetic acid was removed under reduced pressure and the residue extracted with acetone. The material left on evaporation of the acetone was dissolved in methylene chloride and the solution washed with sodium bicarbonate solution. The methylene chloride contained 54 mgm. of neutral material which crystallized from acetone on addition of ether giving 16 mgm., m.p. 182–190°. The infrared spectrum of this proved

identical with that of desmethanolhydroxy*seco*lycoctonam diketone monoacetate. A further 14 mgm. of cruder material, m.p. 180–186°, was obtained from the mother liquor.

Desmethanolhydroxysecolycoctonam Diketone Monoacetate

The compound when crystallized from acetone–ether had m.p. 192–195°, $[\alpha]_D^{22}$ −47° (*c*, 1.50). Found: C, 61.94; H, 6.93; OCH_3, 18.31; acetyl, 8.64. Calc. for $C_{26}H_{35}NO_9$: C, 61.77; H, 6.98; $4OCH_3$, 18.4; acetyl, 8.31. Ultraviolet spectrum: λ_{max} 230–233 mμ (log ε 3.74); λ_{min} 280 mμ (log ε 1.40); λ_{max} 315 mμ (log ε 1.64). Infrared spectrum (61 mgm. 1 ml. in chloroform, 0.1 mm. cell): 3010(42), 2960(43), 2840(23), 1750(90), 1665(84), 1465(46), 1375(54), 1210–40(80), 1110(81), 1050(66), 985(44), 955(49), 910(22), 830(25).

Alkaline Hydrogen Peroxide on the Desmethanol Diketone

Desmethanolhydroxy*seco*lycoctonam diketone acetate (100 mgm.) was dissolved in 5 cc. of methanol and the solution cooled to 0°. A solution of 150 mgm. of potassium hydroxide in 1 cc. of methanol was added, followed by 1 cc. of 30% hydrogen peroxide and 3 cc. of methanol to clarify the solution. This was stirred at 0° for 10 min., diluted with water and extracted with methylene chloride, then acidified and extracted again with methylene chloride. The combined extracts were separated into 92 mgm. of neutral and 6 mgm. of acidic material. Neither product was obtained crystalline.

Strongly Adsorbed Ketone

When crystallized from acetone–ether this melted at 209–213°, $[\alpha]_D^{23}$ −110° (*c*, 2.67). Found: C, 60.15; H, 7.27; OCH_3, 23.2. Calc. for $C_{24}H_{33}O_9N$: C, 59.86; H, 7.33; $4OCH_3$, 25.8.

Ultraviolet spectrum: Shoulders around 230 mμ (log ε 3.0) and 275 mμ (log ε 1.8).

Infrared spectrum (60 mgm. 1 ml. in chloroform, 0.1 mm. cell): 3440(28), 3010(52), 2960(50), 2900(33), 2840(31), 1757(76), 1715(68), 1650(83), 1485(47), 1470(54), 1420(32), 1385(29), 1360(25), 1330(30), 1290(48), 1205–1240(51), 1175(42), 1110(87), 1060(75), 980(47), 910(21).

The compound was recovered unchanged after 16 hr. in acetic anhydride – pyridine (1:1) solution.

ACKNOWLEDGMENT

We are indebted to Dr. R. C. Cookson and Dr. M. Trevett for informing us prior to publication of their observations on hydroxylycoctonine and to Dr. Cookson for his comments on the diterpenoid nature of lycoctonine. We wish to thank Dr. R. N. Jones and Mr. R. Lauzon for obtaining the infrared spectra, and Mr. H. Seguin for the analyses.

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DÉRIVÉS DU TRIMÉTHYL-1,8,8 BICYCLO[3,2,1]OCTANE

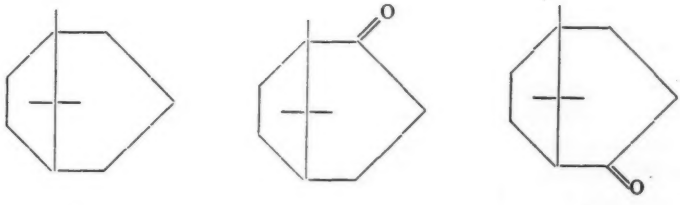
I. LA RÉACTION DU DIAZOMÉTHANE AVEC LA CAMPHOQUINONE[1]

PAR H. FAVRE, B. MARINIER[2] ET J-C. RICHER[2]

RÉSUMÉ

On montre dans ce mémoire que le diazométhane réagit avec la camphoquinone pour donner un mélange de méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 et de méthoxy-4 triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2. Ces éthers cétoénoliques de la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 ont été séparés, leur bromation et leur oximation étudiées, leur dégradation effectuée par réduction par l'hydrure de lithium et d'aluminium suivie d'un traitement acide; on a obtenu respectivement la triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 et la triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2, dont l'hydrogénation de la liaison éthylénique conduit à l'homoépicamphre et à l'homocamphre.

Des difficultés de synthèse ont rendu peu accessibles les dérivés du triméthyl-1,8,8 bicyclo[3,2,1]octane (I), homologue supérieur du bornane. Il nous a paru utile d'entreprendre dans ce domaine une étude systématique et comparée des cétones, des alcools et des amines, dont la fonction se situe sur le chaînon tricarboné. Seules quelques cétones sont connues : l'homocamphre (II) (4, 5, 9), l'homoépicamphre (III) (12) et la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 (IV)[3] (3, 6, 8, 9). Notre premier objectif fut la synthèse des monocétones II et III.



I II III

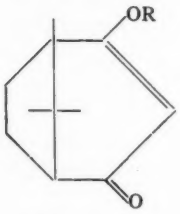
Nous nous sommes inspirés d'un travail de Rupe et Frey (9)[4]; ces auteurs ont préparé l'homocamphre (II) à partir de la camphoquinone par l'intermédiaire de la dictétone IV. Nous avons décidé de mettre en oeuvre cette dicé-

[1]*Manuscrit reçu le 18 mai, 1956.*
Contribution du Département de Chimie de l'Université de Montréal, Montréal, P.Q. Ce mémoire a été présenté au 14e Congrès International de Chimie pure et appliquée, Zurich, 21–27 juillet, 1955; il est tiré, en partie, des mémoires de maîtrise de B. Marinier et J-C. Richer.
[2]*Boursier du Conseil National de Recherches du Canada.*
[3]*Le symbole IV représente l'ensemble des trois structures distinctes IVa (forme dicétonique), IVb et IVc (formes céto-énoliques).*
[4]*Nous avons écarté d'emblée, en raison de leur faible rendement global, les synthèses qui font appel à un procédé de cyclisation pour la formation du noyau bicyclo[3,2,1]octanique, tant pour la synthèse de l'homocamphre (4, 5, 9) et de l'homoépicamphre (12) que pour celle de la dicétone IV (3, 6, 8). Rupe et ses collaborateurs (9, 10) ont montré que l'on pouvait passer d'un seul jet et avec un rendement excellent du noyau bicyclo[2,2,1]heptanique au noyau bicyclo[3,2,1]octanique par un procédé d'extension de cycle.*

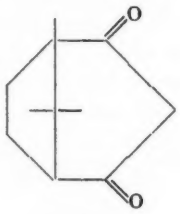
tone IV et d'en tirer deux monocétones, à l'image de la production des cétones $\alpha\beta$-éthyléniques à partir des éthers céto-énoliques des dicétones β alicycliques (1, 2), selon le schéma suivant :

$$-C(OCH_3)=CH-CO- \xrightarrow{LiAlH_4} -C(OCH_3)=CH-CHOH- \xrightarrow{H^+} -CO-CH=CH-.$$

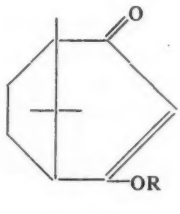
La méthode de Rupe et Frey (9) semblait être particulièrement bien adaptée à notre projet, puisque ces auteurs ont montré que l'action du diazométhane sur la camphoquinone conduit à un mélange des deux éthers céto-énoliques méthyliques de la dicétone IV. Un doute cependant planait sur la structure de ces éthers. D'une part, Rupe et Frey (9) leur assignèrent les structures V*d* et V*c* (correspondant respectivement à un éther solide p.f. 54–55°, $[\alpha]_D^{20} = -29.3°$,[5] de structure soit-disant *trans*, et à un éther liquide, $[\alpha]_D^{20} = +1.1°$, de structure *cis*). Isshiki (3) proposa d'autre part, sans toutefois apporter de preuves à l'appui, les structures V*b* et V*c*, prévues par la théorie pour une dicétone β asymétrique.



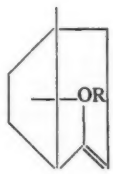
IV*b* R = H
V*b* R = CH_3



IV*a*



IV*c* R = H
V*c* R = CH_3



IV*d* R = H
V*d* R = CH_3

Ces divergences nous ont conduits à reprendre l'étude de l'action du diazométhane sur la camphoquinone. Nous avons trouvé que le mélange brut issu de la réaction se sépare bien, comme l'ont montré Rupe et Häfliger (10) puis Rupe et Frey (9), en un solide p.f. 56°, $[\alpha]_D^{23} = -29.0°$, et un liquide, $[\alpha]_D^{23} = -3.9°$. En soumettant ce liquide à une distillation fractionnée, il est possible d'en retirer, par cristallisation des fractions, deux composés solides : l'un est l'éther p.f. 56°, déjà décrit, l'autre est un éther isomère p.f. 71°, $[\alpha]_D^{23} = +33.9°$.Le mélange de ces deux éthers céto-énoliques constitue 88.5% du mélange brut et le rapport des pourcentages des éthers p.f. 56° (V*c*) et p.f. 71° (V*b*) est d'environ (65–68)/(35–32). Les deux éthers solides sont facilement hydrolysés par l'acide chlorhydrique, à température ambiante, en dicétone IV ; ils se forment tous deux lorsque cette dicétone β réagit avec un excès de diazométhane.

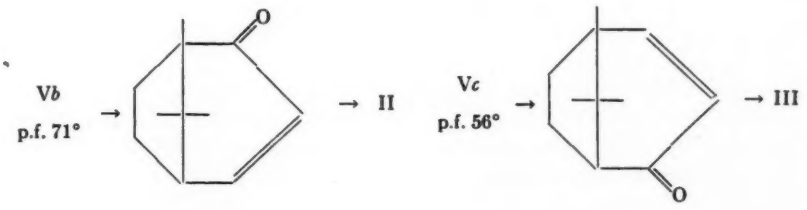
Pour déterminer les positions respectives du carbonyle et du méthoxyle dans les deux isomères p.f. 56° et p.f. 71°, nous avons mis en oeuvre la méthode d'élimination du carbonyle mentionnée plus haut, en appliquant le mode opératoire de Seifert et Schinz (13).

L'isomère p.f. 71° conduit à un mélange complexe, duquel on retire par chromatographie sur alumine 50% environ de triméthyl-1,8,8 bicyclo[3,2,1]oc-

[5]*Toutes les valeurs du pouvoir rotatoire données dans ce mémoire s'entendent pour des solutions benzéniques, sauf indication contraire.*

tène-3 one-2 (VI), dont le point de fusion (174–176°) et le pouvoir rotatoire (−55.3°) sont en bon accord avec les valeurs données par Rupe et Frey (9). La marche de la purification fut suivie par l'analyse de l'absorption dans l'ultraviolet dans la région de 230 mμ et par hydrogénation catalytique de la liaison éthylénique. L'hydrogénation d'échantillons très purs conduit à l'homocamphre (II) p.f. 187–190°, $[\alpha]_D^{23} = -108.9°$, identique à un homocamphre que nous avons préparé selon les indications de Lapworth et Royle (4). L'identité des deux cétones fut démontrée par absorption infrarouge. Le test du point de fusion de mélange, bien que positif, a peu de valeur ; en effet les cétones II et III, ainsi que VI et VII, ne donnent pas de dépression de point de fusion lorsqu'elles sont mélangées entre elles dans les conditions habituelles du test ; l'interprétation des points de fusion et des points de fusion de mélange est ainsi rendue très difficile (voir à ce sujet Pirsch (7)). Le pouvoir rotatoire est le meilleur critérium de pureté ; il est légitime d'admettre que l'homocamphre de Lapworth et Royle (4), en raison de sa méthode de préparation, est un composé pur et exempt d'isomères et par suite de prendre son pouvoir rotatoire comme standard.

On n'arrive à l'homocamphre pur, par dégradation de l'éther céto-énolique p.f. 71°, qu'en effectuant une purification soignée au niveau de la cétone non saturée VI ; la purification—par chromatographie sur alumine, sublimation fractionnée ou passage par la semicarbazone—mise en oeuvre sur des échantillons d'homocamphre issu de la cétone VI brute ou insuffisamment purifiée ne convient pas. Le passage par le semicarbazone a toutefois permis de mettre en évidence une cétone isomère de l'homocamphre, à pouvoir rotatoire fortement lévogyre ; nous n'avons pas pu l'isoler à l'état de pureté.



VI VII

L'isomère p.f. 56°, à son tour, donne naissance à une cétone αβ-éthylénique p.f. 169°, $[\alpha]_D^{23} = -3.3°$, caractérisée comme triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 (VII) : l'oxydation en acide camphorique et en anhydride camphorique montre que le squelette n'a subi aucune variation au cours de la dégradation ; le spectre ultraviolet, par un maximum d'absorption à 233.5 mμ ($\log \epsilon = 3.95$), montre la présence d'un groupement —CO—CH=CH— ; enfin l'hydrogénation catalytique (palladium) en conduisant à l'homoépicamphre (III) p.f. 197–199°, $[\alpha]_D^{23} = +136°$, établit sans ambiguité que le carbonyle est en position γ du radical méthyle placé en tête de pont. Cet homoépicamphre soutient bien la comparaison (analyse infrarouge, point de fusion de mélange, pouvoir rotatoire) avec un homoépicamphre que nous avons

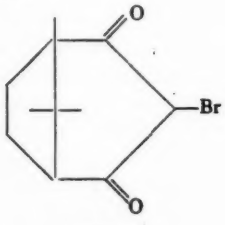
préparé selon le procédé de Salmon-Legagneur (12) et que nous prenons comme standard. Contrairement à la dégradation de l'éther p.f. 71° celle de l'isomère p.f. 56° conduit avec un bon rendement à la cétone $\alpha\beta$-éthylénique VII remarquablement pure et exempte d'isomères.

Ces dégradations font de l'isomère p.f. 71° la méthoxy-4 triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 (V*b*) et de l'isomère p.f. 56° la méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (V*c*). Elles montrent que l'équilibre dicétonique⇄céto-énolique de la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 (IV) s'établit, comme le prévoit la théorie, entre les formes IV*a* ⇄ IV*b* ⇄ IV*c*; on peut de ce fait abandonner les conclusions de Rupe et Frey (9) touchant cet équilibre.

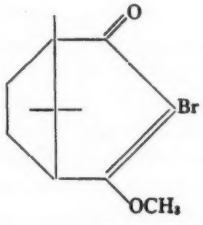
Nous avons étudié l'oximation et la bromation des deux éthers V*b* et V*c*; ces deux points qui figurent dans le mémoire de Rupe et Frey (9) demandaient à être repris, puisque ces auteurs ont considéré comme un éther pur ce qui n'était en fait qu'un mélange des éthers V*b* et V*c*.

L'éther méthylique V*b* p.f. 71° donne facilement une oxime bien cristallisable p.f. 181–183° dans des conditions opératoires ménagées, tandis que l'éther p.f. 56° ne conduit à aucun dérivé cristallisé dans des conditions identiques; il conduit en revanche à la dioxime de la dicétone IV, p.f. 209° déc., dans des conditions plus énergiques. Nous pensons que notre oxime p.f. 181–183° est identique à celle décrite par Rupe et Frey (9), p.f. 185–185.5°; ces auteurs l'avaient obtenue à partir de leur éther liquide. Nous ne pouvons par contre nous prononcer sur la nature de l'oxime p.f. 195–196° qu'ils ont préparée à partir de l'éther p.f. 56°, par suite de l'absence de données, dans leur mémoire (9), au sujet de la composition centésimale de cette oxime.

Rupe et Frey avaient conclu à l'isomérie *cis–trans* de la forme céto-énolique IV*c* et des éthers énoliques correspondants après une étude de l'action du brome sur les éthers méthyliques. Nos résultats confirment ceux de ces auteurs pour la bromation de l'éther p.f. 56° (V*c*) : on obtient bien la dicétone monobromée VIII[6] et l'éther méthylique bromé IX, dont la structure est maintenant certaine. Par contre l'éther p.f. 71° (V*b*) donne, dans des conditions expérimentales identiques, principalement la dicétone monobromée VIII et très peu d'un éther bromé (de 3 à 10% suivant les essais), liquide très instable dont nous n'avons pas poursuivi l'étude; il se transforme de lui-même en dicétone monobromée VIII.



VIII



IX

[6]*On peut envisager pour cette dicétone bromée deux formes céto-énoliques qui correspondraient aux formes IVb et IVc de la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4.*

PARTIE EXPÉRIMENTALE[7]

1. Réaction du diazométhane avec la camphoquinone

1.1. Camphoquinone

Elle a été préparée à partir d'un camphre chinois en poudre, p.f. 179–180°, $[\alpha]_D^{23} = +42.6°$ ($c = 1.21$; éthanol 95%), selon le mode opératoire de Rupe et Tommasi di Vignano (11). Elle présentait les constantes suivantes : p.f. 198.5–199°, $[\alpha]_D^{23} = -106.5°$ ($c = 15$; benzène).

1.2. Séparation des éthers isomères p.f. 56° (Vc) et p.f. 71° (Vb)

Séparation A.—583 g. (99.5% de la théorie) du mélange brut résultant de la réaction de 500 g. de camphoquinone (par portions de 20 g.) avec la quantité requise de diazométhane, selon les indications de Rupe et Frey (9), furent rectifiés dans un ballon de Claisen tout en faisant passer un courant d'azote par le capillaire : (*a*) 10.1 g. p.é. jusqu'à 151°, 18 mm. (têtes) ; (*b*) 540.3 g., p.é. 151–156°, 18 mm., légèrement jaune, $[\alpha]_D^{23} = -8.8°$ ($c = 10.0$; benzène) ; (*c*) résidu, 26 g.

Séparation B.—511.8 g. de la fraction (*b*) obtenue au cours de la séparation *A* furent abandonnés à 10–12° ; au bout de quelques jours on a isolé par essorage 68.7 g. de méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (Vc) brute fondant à 48–51°, qui recristallisée dans l'éther de pétrole (p.é. 40–60°) se présente sous forme de gros prismes incolores p.f. 56°, $[\alpha]_D^{23} = -29.7°$ ($c = 4.03$; benzène) ou $-29.0°$ ($c = 10$; benzène). Calculé pour $C_{12}H_{18}O_2$: C, 74.19 ; H, 9.34%. Trouvé : C, 74.52 ; H, 9.40%. Litt. : (9) p.f. 54–55°, $[\alpha]_D^{20} = -29.3°$ ($c = 10$; benzène). *Spectre ultraviolet* : λ_{max} 250 mμ ; $\log \epsilon = 4.13$ (éthanol 95%). Liquide résiduel, $[\alpha]_D^{23} = -3.9°$ ($c = 10.0$; benzène).

Séparation C.—252 g. de liquide résiduel obtenu au cours de la séparation *B* après essorage furent rectifiés à travers une colonne de Vigreux, en atmosphère d'azote : fractions 1–2, 28 g., p.é. jusqu'à 83°, 0.2 mm. ; fractions 3–7, 106.5 g., p.é. de 78 à 87°, 0.2 mm. ; fractions 8–9, 43.4 g., p.é. de 82 à 88°, 0.15 mm. ; fractions 10–12, 58.3 g., p.é. de 85 à 93, 0.15 mm. ; fraction 13, 3 g., p.é. 90–93°, 0.15 mm. ; résidu, 3.1 g. Les fractions 1, 2, 8 et 9 ne se cristallisèrent pas. Les fractions 3–7 se cristallisèrent partiellement ; par essorage on a obtenu 31.9 g. de méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (Vc) brute, qui après cristallisation dans l'éther de pétrole fondait à 56°, seule ou en mélange avec l'éther p.f. 56° obtenu au cours de la séparation *B*. Les fractions 10–12 se cristallisèrent en partie ; par essorage on a obtenu 26.2 g. de fines aiguilles p.f. brut 61–67° auxquels on ajouta les 3 g. de la fraction 13 qui se cristallisa totalement, p.f. brut 65–68°. Cette méthoxy-4 triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 brute (Vb) se présente, après cristallisation dans l'éther de pétrole (p.é. 40–60°), sous forme d'aiguilles incolores, p.f. 71°, $[\alpha] = {}_D^{23} +33.4°$ ($c = 4.02$; benzène) ou $+33.9°$ ($c = 10$; benzène). Calculé pour $C_{12}H_{18}O_2$: C, 74.19 ; H,

[7]*Les points de fusion (p.f.) ne sont pas corrigés; ils ont été déterminés dans un appareil de Thiele. Les spectres infrarouges ont été déterminés à l'aide d'un spectromètre "Perkin-Elmer", modèle 112, à simple faisceau et parcours double; les spectres ultraviolets à l'aide d'un spectromètre "Beckman" DU. Les analyses ont été faites, les unes par Geller Microanalytical Laboratories, Hackensack, N.J., les autres par nos soins (les valeurs sont alors marquées d'un*).*

9.34%. Trouvé: C, 74.07; H, 9.33%. *Spectre ultraviolet*: λ_{max} 253.5 mμ; log ϵ = 4.15 (éthanol 95%). Les fractions 3–7 et 10–12, débarassées de leurs cristaux, et les fractions 8 et 9, restées liquides, furent soumises à une série de quatre distillations et de quatre cristallisations faites alternativement qui permit de retirer des 252 g. initiaux: (*a*) 68 g. de l'éther V*c* pur, p.f. 56°; (*b*) 49 g. de l'éther V*b* pur, p.f. 71°.

1.3. Triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 (IV)

Dix grammes du mélange liquide résultant de l'action du diazométhane sur la camphoquinone, en solution dans 50 ml. d'éther, sont agités durant 12 h., à 25°, avec 50 ml. d'HCl 15%. La phase aqueuse est décantée et extraite deux fois par de l'éther. Les parties acides sont extraites des solutions éthérées réunies par 30 ml. de NaOH 10%. Par acidification de la solution alcaline par HCl conc. (rouge congo), la dicétone β se précipite. On l'essore et la lave deux fois avec un peu d'eau glacée. On obtient 7.2 g. de produit brut, p.f. 215–220°. Un échantillon a été cristallisé dans le benzène: fines aiguilles blanches, fondant à 220–222°, $[\alpha]_D^{23} = -7.7°$ (c = 4.02; benzène). Calculé pour $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%. Trouvé: C, 73.53; H, 9.04%. La dicétone se sublime (11 mm., 150–160°); elle fond alors à 220–221°. Litt.: (9) p.f. 218–222°; $[\alpha]_D^{20} = -8.8°$ (c = 10; benzène); (3) p.f. 222–224°.

Dioxime.—Cristaux blancs, p.f. 209–209.5° déc., cristallisée dans l'éthanol aqueux, $[\alpha]_D^{23} = -2.0°$ (c = 1.0; éthanol anhydre; tube 4 dm.). Calculé pour $C_{11}H_{18}O_2N_2$: N, 13.33%. Trouvé: N, 13.21%*. Litt.: (9) p.f. 209° déc.

1.4. Composition du mélange réactionnel brut obtenu en 1.2

L'hydrolyse par HCl 15% de toutes les fractions liquides (provenant de la fraction (*a*) de la séparation *A*, des liquides résiduels des essorages effectuées au cours des séparations *B* et *C*) a abandonné un résidu (32 g.) non hydrolysable, liquide jaune, dont l'étude n'a pas été poursuivie. 500 g. de camphoquinone ont ainsi donné 517.6 g. (88.5% de la théorie) du mélange des éthers V*b* et V*c*; on peut estimer, par l'analyse du pouvoir rotatoire de la fraction(*b*) séparation *A*, et du mélange obtenu après essorage séparation *B*, que les pourcentages respectifs des éthers V*c* et V*b* sont les suivants: 65–68% d'éther V*c* pour 35–32% d'éther V*b*.

1.5. Action du diazométhane sur la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 (IV)

A une solution de 70 g. de dicétone IV dans 500 ml. de benzène et 30 ml. de méthanol, refroidie à 6°, on ajoute une solution éthérée de diazométhane jusqu'à coloration jaune persistante. Les solvants sont distillés sous pression réduite, le résidu liquide repris par de l'éther; la solution éthérée est lavée à la soude pour éliminer la dicétone β qui n'aurait pas réagi, puis à l'eau jusqu'à neutralité. On sèche et distille l'éther. On recueille 71.6 g. (95% de la théorie) d'un liquide incolore et inodore, distillant sans laisser de résidu entre 87° et 90° sous 0.3 mm., $[\alpha]_D^{23} = 0°$ (c = 10; benzène); d'après le pouvoir rotatoire on a en main un mélange contenant 53.9% de l'éther méthylique V*c* et 46.1% de l'éther méthylique V*b*.

Après trois distillations fractionnées (11 mm., colonne de Vigreux, atmosphère d'azote), on obtient :

(*a*) 28.5 g. d'éther V*c* brut, p.f. 48–54° montant à 56° par cristallisation ;

(*b*) 23.4 g. d'éther V*b* brut, p.f. 63–71° passant à 71° après cristallisation ;

(*c*) 12.4 g. de mélange résiduel, hydrolysé par HCl à la manière habituelle en dicétone IV.

2. Étude de la méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (éther V*c*) et de la méthoxy-4 triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 (éther V*b*)

2.1. Hydrolyse

Mode opératoire utilisé précédemment en 1.3 :

(*a*) 0.5 g. d'éther V*c* ont donné 0.370 g. (80%) de la dicétone IV, p.f. 220–221° par sublimation. Litt. : (9) p.f. 218–222° ;

(*b*) 0.5 g. d'éther V*b* ont donné 0.355 g. (77%) de la dicétone IV, p.f. 219–220° par sublimation, ne donnant pas de dépression de p.f. en mélange avec celle obtenue en (*a*).

Dans les deux cas il n'y a pas de résidu d'hydrolyse ; nous n'avons pas cherché à récupérer la dicétone IV manquante des solutions aqueuses intervenant au cours de l'hydrolyse, ce qui explique les rendements de l'ordre de 80% ; il est possible de récupérer quantitativement la dicétone IV en extrayant les solutions aqueuses par du chloroforme.

2.2. Oximation

Méthode A.—Un mélange de 1 g. de l'éther V*b* (ou V*c*), 0.7 g. de chlorhydrate d'hydroxylamine et 1.5 ml. de pyridine anhydre est abandonné à température ambiante pendant 12 h., puis chauffé sur un bain-marie pendant une heure. Par addition d'eau :

(*a*) dans le cas de l'éther V*c* il se précipite une huile dont aucun dérivé cristallisé n'a pu être isolé ;

(*b*) dans le cas de l'éther V*b* il se forme un précipité qui recristallisé dans l'éthanol aqueux fournit l'oxime de l'éther V*b*, paillettes blanches p.f. 181–183° déc. Calculé pour $C_{12}H_{19}O_2N$: N, 6.70%. Trouvé : N, 6.87%*.

Méthode B.—Un mélange de 1 g. de l'éther V*c*, 0.7 g. de chlorhydrate d'hydroxylamine et 1.5 ml. de pyridine anhydre est chauffé sur un bain-marie durant huit heures. Après refroidissement on ajoute 1 ml. d'eau et abandonne à la glacière pendant 12 h. La dioxime de la triméthyl-1,8,8 bicyclo[3,2,1]octanedione-2,4 précipite par addition d'éther de pétrole. Après cristallisation dans l'éthanol aqueux elle fond à 209° déc., $[\alpha]_D^{23} = -1.9°$ ($c = 1.00$; éthanol anhydre ; tube 4 dm.). Elle donne une dépression de p.f. de 1° à 2° en mélange avec la dioxime préparée auparavant en 1.3 ; les spectres infrarouges (dioxime mouillée d'huile de paraffine, prisme NaCl) sont pratiquement identiques. Calculé pour $C_{11}H_{18}O_2N_2$: N, 13.33%. Trouvé : N, 13.12%*.

2.3. Bromation

Effectuée en suivant exactement les données de Rupe et Frey (9) :

(*a*) 2 g. d'éther V*c* ont donné 1.5 g. de neutres correspondant à la bromo-3 méthoxy-4 triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (IX) aiguilles incolores

cristallisées dans l'éther de pétrole (p.é. 40–60°), p.f. 103–104°, $[\alpha]_D^{23} = +30.0°$ ($c = 10.0$; benzène). Calculé pour $C_{12}H_{17}O_2Br$: Br, 29.26%. Trouvé: Br, 29.00%. Litt.: (9) p.f. 104°. *Spectre ultraviolet*: λ_{max} 275 mμ; log ε = 4.05 (éthanol 95%), et 1 g. de parties acides (bromo-3 triméthyl-1,8,8 bicyclo[3,2,1] octanedione-2,4 (VIII)), p.f. 188–189°. Litt.: (9) p.f. 187–188°.

(*b*) 4 g. d'éther V*b* ont donné 4.64 g. de dicétone monobromée VIII, p.f. 188–189°, et 0.2 g. de parties neutres, liquide jaune pâle, ne se cristallisant pas et se décomposant rapidement pour donner la dicétone monobromée p.f. 188–189°. Le pourcentage de parties neutres variait légèrement (de 3 à 10%) dans les quelques essais effectués.

2.4. Dégradation de l'éther Vc

2.41. Triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 (VII)

Une solution de 20 g. (0.1 mole) de l'éther V*c* dans 100 ml. d'oxyde d'éthyle anhydre est introduite goutte à goutte, sous bonne agitation, à 3.4 g. (0.09 mole) de $LiAlH_4$ finement pulvérisé en suspension dans 200 ml. d'oxyde d'éthyle anhydre. On chauffe ensuite 30 min. à l'ébullition à reflux, puis, en refroidissant à 0°, on ajoute 16 ml. d'eau. Le tout est alors versé sur 44 g. de glace concassée; on ajoute lentement, en agitant, 60 ml. d'H_2SO_4 conc., de façon à ce que la température du mélange en réaction ne dépasse pas −6° (durée de l'opération: de cinq à six heures). La couche aqueuse est décantée et extraite par de l'éther; les solutions éthérées réunies sont lavées à l'eau, au carbonate de sodium et à l'eau jusqu'à neutralité. On sèche et évapore très lentement l'éther à travers une colonne de Widmer. On recueille 16.6 g. (98 % de la théorie) d'un solide blanc, à odeur camphrée, très facilement sublimable. Après une sublimation on a: (*a*) 15.6 g. (92%) de triméthyl-5,8,8 bicyclo[3,2,1] octène-3 one-2, p.f. 167.5–169°, $[\alpha]_D^{23} = -1.5°$ ($c = 4.08$; benzène); (*b*) 1 g. d'un composé p.f. supérieur à 220° que l'on écarte. 6.468 g. de la fraction (*a*), par chromatographie sur 198 g. d'alumine (alumine Merck pour chromatographie), donnent: fraction 1, 0.199 g. d'huile éluée par de l'éther de pétrole; fractions 2–45, 5.357 g. (83%) de triméthyl-5,8,8 bicyclo[3,2,1]octène-3 one-2 (VII) dont un échantillon analytique présente les constantes suivantes: p.f. 169°, $[\alpha]_D^{23} = -3.3°$ ($c = 4.01$; benzène). Calculé pour $C_{11}H_{16}O$: C, 80.44; H, 9.82%. Trouvé: 80.15; H, 9.86%. *Spectre ultraviolet*: λ_{max} 233.5 mμ; log ε = 3.95 (éthanol 95%).

Oxime.—Cristallise en aiguilles blanches dans le méthanol aqueux, p.f. 91°. Calculé pour $C_{11}H_{17}ON$: C, 73.70; H, 9.56; N, 7.82. Trouvé: C, 73.37; H, 9.76; N, 7.90%*.

Dinitro-2,4 phénylhydrazone.—Cristallisée dans le méthanol; paillettes rouges, p.f. 167–167.5°. Calculé pour $C_{17}H_{20}O_4N_4$: C, 59.29; H, 5.85; N, 16.27%. Trouvé: C, 59.38; H, 5.86; N, 16.41%*.

Semimicro-hydrogénation.—164 mg. de la cétone VII, dans 8 ml. d'éthanol 95%, ont fixé 24.8 ml. d'hydrogène en présence de 150 mg. d'un catalyseur de palladium sur carbonate de calcium (2%) hydrogéné au préalable. Calculé: 24.8 ml. (748 mm., 25°).

Oxydation.—On ajoute à 0.5 g. de cétone VII en solution dans 1.5 ml. d'acide

acétique glacial 13.8 ml. d'une solution préparée en dissolvant 4 g. de CrO_3 dans 20 ml. d'acide acétique glacial et 4 ml. d'eau. On chauffe 30 min. sur un bain-marie, laisse reposer 12 h. puis verse sur de l'eau. On extrait soigneusement à l'éther, on sèche la couche éthérée évapore l'éther à pression ordinaire et la plus grande partie de l'acide acétique sous vide. On reprend alors par de l'éther et sépare le mélange en parties acides et parties neutres, à la manière habituelle. On isole 148 mg. d'acide camphorique p.f. 182.5–183°, seul ou en mélange avec de l'acide camphorique authentique, et 238 mg. de parties neutres dont on retire par dissolution fractionnée dans l'éther de pétrole 24 mg. d'anhydride camphorique p.f. 218–222°, seul ou en mélange avec de l'anhydride camphorique authentique.

2.42. Homoépicamphre (III)

Un gramme de cétone $\alpha\beta$-éthylénique VII, $[\alpha]_D^{23} = -3.3°$ ($c = 4.01$; benzène), dans 35 ml. d'éthanol 95% sont agités dans de l'hydrogène en présence de 750 mg. de catalyseur ($Pd/CaCO_3$, 2%). En 80 min. 160 ml. d'H_2 sont fixés (calculé: 152 ml., 747 mm., 25°). Après distillation très lente de l'alcool à travers une colonne de Widmer on retrouve 890 mg. (89% de la théorie) d'homoépicamphre qui après sublimation présente les constantes suivantes: p.f. 197–199°, $[\alpha]_D^{23} = +136.0°$ ($c = 4.0$; benzène). Calculé pour $C_{11}H_{18}O$: C, 79.46; H, 10.91%. Trouvé: C, 79.40, 79.19; H, 10.97, 11.12%. Il n'y a pas d'abaissement du p.f. de ce composé en mélange avec un homoépicamphre analytiquement pur préparé selon la méthode de Salmon-Legagneur p.f. 198.5–199°, $[\alpha]_D^{23} = +130.7°$ ($c = 4.02$; benzène). Salmon-Legagneur indique (12): p.f. 202–204°, $[\alpha]_D^{20} = +130.3°$ ($c = 7.862$; benzène). Les spectres infrarouges des deux cétones sont identiques; la bande C=O apparaît à 1716 $cm.^{-1}$ (fluorolube, prisme NaCl ou CaF_2).

Oxime.—Obtenue en chauffant à l'ébullition à reflux l'homoépicamphre avec du chlorhydrate d'hydroxylamine dans de l'alcool aqueux contenant 2% d'hydroxyde de sodium; elle cristallise en fines aiguilles blanches p.f. 104–105°, $[\alpha]_D^{23} = +124°$ ($c = 3.9$; benzène). Calculé pour $C_{11}H_{19}ON$: N, 7.74%. Trouvé: N, 7.54%*. Cette oxime ne donne pas de dépression de p.f. en mélange avec l'oxime préparée dans des conditions identiques à partir de l'homoépicamphre obtenu selon Salmon-Legagneur. Alors que Salmon-Legagneur (12) indique pour cette oxime $[\alpha]_D^{24} = +108.5°$ ($c = 3.87$; méthanol) nous avons trouvé $[\alpha]_D^{23} = +125.6°$ ($c = 3.91$; méthanol); le p.f. est pourtant bien de 104–105° comme indiqué dans le mémoire (12).

Dinitro-2,4 phénylhydrazone.—Cristallisée dans un mélange d'éthanol et d'acétate d'éthyle; paillettes orange p.f. 178°. Calculé pour $C_{17}H_{22}O_4N_4$: N, 16.18%. Trouvé: N, 16.03%*.

2.5. Dégradation de l'éther Vb

2.51. Triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (VI)

Le mode opératoire est le même que celui décrit en 2.41. 27.7 g. (0.143 mole) de l'éther *Vb* sont réduits par 4.7 g. (0.123 mole) de $LiAlH_4$. Après déshydratation par l'acide sulfurique conc. (83 ml.) et extraction on obtient 22.2 g.

(95% de la théorie) de triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 brute, p.f. 178–180°, $[\alpha]_D^{23} = -52.9°$ ($c = 10.0$; benzène). 20.9 g. de la cétone brute sont sublimés plusieurs fois sous 8–10 mm., à 120–130°; les diverses fractions sont rassemblées en deux fractions principales: fraction *A*—15.4 g. comprenant les fractions p.f. 176–178°, pouvoir rotatoire voisin de −58°, et les fractions p.f. 177–179°, pouvoir rotatoire voisin de −56°; fraction *B*—5.21 g. très nombreuses fractions dont les p.f. sont compris entre 165 et 205°.

La chromatographie sur alumine (alumine Merck pour chromatographie) de 10.2 g. provenant de la fraction *A* donne: 1.289 g. p.f. 173°, $[\alpha]_D^{23} = -67.4°$ (élution par l'éther de pétrole); 6.153 g. de triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 (VI) (élution par l'éther de pétrole); 1.7 g. comprenant diverses fractions, huiles dont le pouvoir rotatoire varie entre −50° et +27°.[8]

La triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 fond à 174–176°, $[\alpha]_D^{23} = -55.3°$ ($c = 5.14$; benzène). Calculé pour $C_{11}H_{16}O$: C, 80.44; H, 9.82%. Trouvé: C, 80.36; H, 9.91%. Litt.: (9) p.f. 173–175°, $[\alpha]_D^{20} = -51.9°$ ($c = 10$; benzène). *Spectre ultraviolet*: λ_{max} 231 mμ; log ε = 3.98 (éthanol 95%).

Oxime.—Fines aiguilles incolores, cristallisées dans l'éthanol aqueux, p.f. 146–147°, $[\alpha]_D^{23} = -104.2°$ ($c = 3.49$; méthanol). Calculé pour $C_{11}H_{17}ON$: N, 7.82%. Trouvé: N, 7.92%*. Litt.: (9) p.f. 143.5–145°.

Dinitro-2,4 phénylhydrazone.—Paillettes rouge-orangé, cristallisées dans un mélange d'acide acétique et de méthanol, p.f. 197–198.5°. Calculé pour $C_{17}H_{20}O_4N_4$: N, 16.27%. Trouvé: N, 16.03%*. Litt.: (9) p.f. 181–184°.

Semimicro-hydrogénation.—159.8 mg. de triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 en solution dans 8 ml. d'éthanol 95%, en présence de 150 mg. de catalyseur (palladium/carbonate de calcium, 2%) hydrogéné au préalable, ont fixé 24.2 ml. d'H_2; calculé pour 1 H_2: 24.0 ml. (755 mm., 25°).

Oxydation.—Mode opératoire, comme en 2.41. 1 g. de triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2 ont donné 400 mg. d'acide camphorique p.f. 185° et 15 mg. d'anhydride camphorique p.f. 218–220°. Identité prouvée par p.f. de mélange.

2.52. Homocamphre (II)

(A) La semimicro hydrogénation de la triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2, $[\alpha]_D^{23} = -55.3°$ ($c = 5.14$; benzène), décrite en 2.51 conduit à un homocamphre qui présente les constantes suivantes: p.f. 187–190°, $[\alpha]_D^{23} = -108.9°$ ($c = 4.08$; benzène). Calculé pour $C_{11}H_{18}O$: C, 79.46; H, 10.91. Trouvé: C, 79.66, 79.70; H, 10.93, 11.14%. Il n'y a pas de dépression de p.f. lorsque cet homocamphre est mélangé avec un homocamphre préparé selon Lapworth et Royle (4); ce dernier présente les constantes suivantes p.f. 191–193°, $[\alpha]_D^{23} = -111.9°$ ($c = 3.41$; benzène), déterminées sur un composé analytiquement pur. Lapworth et Royle indiquent: p.f. 189–190°; $[\alpha]_D = -112.9°$ ($c = 4.0$; benzène). Les spectres infrarouges des homocamphres préparés par les deux méthodes sont identiques; la bande C=O apparaît à 1709 $cm.^{-1}$ (fluorolube).

Oxime.—p.f. 166.5–167.5°. Litt.: (4) p.f. 167–168°; (9) p.f. 165°.

Dinitro-2,4 phénylhydrazone.—p.f. 238–239°. Litt.: (5) p.f. 232°; (9) p.f. 232–233°.

[8]*Pouvoirs rotatoires déterminés en solution benzénique, c = 4.0.*

(B) 7.8 g. de triméthyl-1,8,8 bicyclo[3,2,1]octène-3 one-2, de pouvoir rotatoire voisin de $-67°$ ($c = 4$; benzène) sont dissous dans 80 ml. d'éthanol 95% et secoués en atmosphère d'hydrogène en présence de 7.5 g. de catalyseur (palladium/carbonate de calcium, 2%). 850 ml. d'H_2 sont fixés en 50 minutes; calculé pour 1 H_2: 1175 ml. (753 mm., 25°). On isole à la manière habituelle 7.2 g. (92% de la théorie) d'homocamphre brut qu'une chromatographie sur alumine (alumine Merck pour chromatographie) permet de séparer en: (*a*) 4.99 g. de solide de pouvoir rotatoire variant entre -121 et $-129°$ ($c = 4$; benzène); (*b*) 2.37 g. fractions liquides. 4.4 g. de la fraction obtenue en (*a*) dans 30 ml. d'éthanol sont traités par 5.4 g. de chlorhydrate de semicarbazide et 8.0 g. d'acétate de sodium dans 15 ml. d'eau à l'ébullition à reflux pendant quatre heures. On obtient après refroidissement à 0° 2.49 g. de semicarbazone brute p.f. 257–259°[9] et 2.58 g. de cétone qui n'a pas réagi. La semicarbazone brute est cristallisée dans l'éthanol aqueux et fractionnée en:

(*a*) Poudre microcristalline p.f. 240–242° qui par hydrolyse par HCl conc. (selon (4)) fournit un homocamphre p.f. 196–197.5°, $[\alpha]_D^{23} = -122°$ ($c = 3.75$; benzène). Calculé pour $C_{11}H_{18}O$: C, 79.46; H, 10.91%. Trouvé: C, 79.17; H, 10.77%. *Spectre infrarouge* (huile de paraffine): pratiquement identique à celui de l'homocamphre dont $[\alpha]_D^{23} = -111.9$ (benzène).

(*b*) Poudre microcristalline p.f. 275° qui par hydrolyse par HCl conc. conduit à un homocamphre p.f. 193.5–195°, $[\alpha]_D^{23} = -152.4°$ ($c = 3.27$; benzène). Calculé pour $C_{11}H_{18}O$: C, 79.46; H, 10.91%. Trouvé: C, 78.97; H, 10.72%. *Spectre infrarouge* (huile de paraffine): pratiquement identique à celui obtenu en (*a*).

2.53. Points de fusion de mélange

Déterminés sur des mélanges 1:1. Homocamphre p.f. 191–193°—homo-épicamphre p.f. 197–199°: fondent à 194°. Cétone VI p.f. 174–176°—cétone VII p.f. 169°: fondent à 172–172.5°.

REMERCIEMENTS

Nous tenons à adresser au Conseil National de Recherches du Canada nos remerciements pour l'aide financière qu'il nous a accordée sous forme de subvention (H.F.) et de bourses d'études (B.M. et J-C.R.). Nous remercions aussi M. le Professeur Sandorfy de l'aide qu'il a bien voulu nous donner en mesurant et en interprétant les spectres infrarouges.

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[9]*Lapworth et Royle donnent pour la semicarbazone pure de l'homocamphre: p.f. 250–252° (4).*

LIGHT ABSORPTION STUDIES

PART III. STRUCTURE AND LIGHT ABSORPTION OF TRISUBSTITUTED BENZENE DERIVATIVES[1]

By W. F. Forbes and W. A. Mueller

ABSTRACT

The spectra of a number of trisubstituted benzene derivatives which have recently been described by Doub and Vandenbelt are discussed in terms of the electronic and steric effects. The assumption of Doub and Vandenbelt, that the steric effects are usually small in absorption spectra, is criticized.

INTRODUCTION

In a recent publication, Doub and Vandenbelt (9) have recorded the ultraviolet light absorption properties of a number of trisubstituted benzene derivatives and discussed these assuming that steric effects are usually small in absorption spectra. Doub and Vandenbelt chose β-resorcylic acid (2,4-dihydroxybenzoic acid) as a representative example and conclude that its spectrum can be explained from the three constituent disubstituted compounds, namely salicylic acid, resorcinol, and *p*-hydroxybenzoic acid. They suggest that the first primary band of salicylic acid (λ_{max} 237 mμ) has no analogue in the spectrum of β-resorcylic acid and note that the inflection (secondary band) of *p*-hydroxybenzoic acid disappears in the spectrum of the trisubstituted compound. More generally they note that frequently the secondary and first primary bands of constituent compounds do not appear at all in the spectrum of the trisubstituted compound.

We have recently reported (10, 11) the spectral properties of a series of substituted acetophenones and benzoic acids, and have shown that the absorption properties exhibited by most *ortho*-substituted benzene derivatives can be explained in terms of steric interference between the two substituents. This work itself was based on a series of previous papers (for example 2, 3, 14).

The present communication re-examines the spectra of some of the trisubstituted benzene derivatives in the light of these hypotheses of steric hindrance.

ULTRAVIOLET ABSORPTION SPECTRA

First Primary Band (B-band)

Our assumptions are as follows:

(i) *ortho*-Disubstituted benzene derivatives in neutral solution would have approximately the same spectra as *para*-isomers but for steric hindrance of resonance (see Table I).

(ii) Ultraviolet light absorption is very sensitive to steric effects: (*a*) slight steric effects give rise to intensity changes *only*; (*b*) larger steric effects give rise

[1]*Manuscript received November 9, 1955.*
Contribution from the Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland. This paper is dedicated to the memory of the late Professor E. A. Braude, D. Sc., F.R.I.C.

to wave-length changes accompanied by changes in the intensity of absorption; this type of steric effect occurs most frequently (see Table II); (*c*) large type steric effects inhibit conjugation almost completely and the molecule absorbs as two distinct entities.

TABLE I

ABSORPTION SPECTRA OF ORTHO- AND PARA-SUBSTITUTED COMPOUNDS IN ABSOLUTE ETHANOL, STERIC EFFECTS ABSENT OR SMALL

Wave-lengths and intensities of the B-band maxima

Compound	Position of substituent			
	Ortho		Para	
	$\lambda_{max.}$ mμ	ϵ_{max}	$\lambda_{max.}$ mμ	ϵ_{max}
Fluoroacetanilide*	239	12,600	240	13,100
Methylbenzaldehyde†	251	13,000	251	15,000

*Ref. 19.
†Ref. 3.

TABLE II

ABSORPTION SPECTRA OF ORTHO- AND PARA-SUBSTITUTED COMPOUNDS IN ABSOLUTE ETHANOL, STERIC EFFECTS PRESENT

Wave-lengths and intensities of the B-band maxima

Compound	Position of substituent			
	Ortho		Para	
	$\lambda_{max.}$ mμ	ϵ_{max}	$\lambda_{max.}$ mμ	ϵ_{max}
Fluorobenzoic acid*	223	9,500	228	11,000
Toluic acid†	228	5,000	236	14,000
Hydroxybenzoic acid†	236	7,500	251	12,500
Anisic acid†	230	6,000	258	11,000
Methylacetanilide‡	230	6,500	245	15,000
Chloroacetanilide‡	240	10,500	249	18,000
Bromoacetanilide‡	234	7,500	252	18,500
Methoxyacetanilide‡	244	10,500	249	15,000
Methylacetophenone§	242	8,500	252	15,000

*Part II, Ref. 11.
†Values in 95% ethanol, Ref. 17.
‡Ref. 19.
§Part I, Ref. 10.

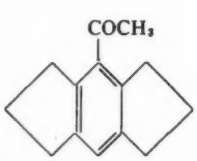
The first assumption is important because later comparisons are based on it, and it is apparently not accepted by Doub and Vandenbelt. Our contention, however, is that it is correct, although not readily obvious, because light absorption properties are such a sensitive indication of steric hindrance. Thus very few *ortho*-substituted benzene derivatives will show a complete absence of steric effects, and similar spectra in *ortho*- and *para*-compounds are only obtained or nearly obtained where the substituent is unusually small (see

Table I). Trisubstituted benzene derivatives of the type discussed by Doub and Vandenbelt will therefore almost invariably give rise to appreciable steric effects.

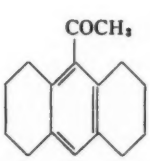
Our second supposition, or rather part (*b*) thereof, is however the key to a more complete understanding of the spectra of this type of derivative and will therefore be now discussed rather more fully. The type of change mentioned—wave-length changes to shorter wave-length accompanied by decreased absorption intensity—is almost the "hallmark" of steric interference in the first primary absorption band of spectra involving the interaction of π–π electrons. Not only does it occur widely in substituted benzene derivatives (see Table II for a few examples), but it is also generally accepted as the explanation of the observed spectra of diphenyls which have been investigated and discussed in some detail by Rodebush and others (3, 4, 12, 16, 18, 20).

Diphenyl absorbs at 249 mμ, ϵ = 15,000, while *o*-methyldiphenyl absorbs at 237 mμ, ϵ = 10,500 (steric effect of type (*b*)). In *o*-*o'*-ditolyl the B-band almost completely vanishes and the absorption closely resembles that of toluene. The latter may be taken as an example of a steric effect of type (*c*), an effect which also may account for the disappearance of some of the bands of partial chromophores in trisubstituted benzene derivatives. Complete disappearance of a band may, however, require a second *ortho*-substituent (we are grateful to a referee of Part II (11) for drawing our attention to a paper by Klevens and Platt (15) who have made this observation in their study of *ortho*-substituted N,N-dimethylanilines).

Any explanation of these observed changes, based entirely on electrical effects, must be ruled out, since the B-bands of the spectra of 4-acetylhydrindacene (I) and 9-acetyloctahydroanthracene (II), for example, are entirely dissimilar (10). On the basis of electrical effects alone, they would be expected to have similar properties.



I, λ_{max} 252 mμ, ϵ = 7000



II, λ_{infl} 220 mμ, ϵ = 10,000

The application of these principles to trisubstituted benzene derivatives can now be attempted and following Doub and Vandenbelt we shall discuss in detail the spectrum of β-resorcylic acid and related compounds. These are listed in Table III.

We have assumed that, as a result of steric interference, conjugation between the two parts of the molecule is decreased; hence a hypsochromic shift accompanied by reduced absorption intensity, relative to the corresponding *para*-substituted compound, is observed. In this manner, the position of the primary band of salicylic acid with respect to *p*-hydroxybenzoic acid may be satisfactorily explained. Salicylic acid may therefore not be directly compared

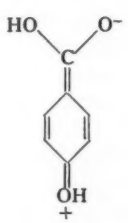
TABLE III

MAIN ABSORPTION MAXIMA OF β-RESORCYLIC ACID AND RELATED COMPOUNDS IN 0.1 *N* HCl

	λ_{max}, mμ	ϵ_{max}		λ_{max}, mμ	ϵ_{max}
Benzoic acid† (in ethanol)	227 271	11,000 760	Salicylic acid*	237 303	9,000 3,600
p-Hydroxybenzoic acid*	255 273 (inflection)	14,100	β-Resorcylic acid*	256 295	13,600 5,500

*Ref. 9.
†Part II, Ref. 11.

with benzoic acid, since then the electrical effect of the OH-substituent, which increases resonance contributions of type III, would be neglected. Therefore salicylic acid compared to benzoic acid gives rise to a slight bathochromic shift, while compared to *p*-hydroxybenzoic acid the expected hypsochromic shift is observed. The analogue of the 237 mμ band in salicylic acid is therefore the 255 mμ band of *p*-hydroxybenzoic acid, which has been shown to be almost



III

identical with the 256 mμ band of β-resorcylic acid (see Table III). The almost identical character of the last two compounds suggests that in β-resorcylic acid the *ortho*-hydroxyl group does not contribute appreciably to the observed spectrum, but exact comparison is not possible, since the exact reference compound, which would require two non-interfering hydroxyl groups in the *para*-position, does not exist.

It would be an oversimplification, however, to say that in β-resorcylic acid the carboxyl group is subject to about the same steric interference from the *ortho*-hydroxyl group as that prevailing in salicylic acid. This would not take into account the increased double bond character of the carbon–carbon link joining the carboxyl group to the benzene ring, due to resonance contributions of type III. The sensitivity of this B-band to increased double-bond character has already been briefly discussed (10) in connection with the spectra of 2,4,6-trimethyl- and 2,3,4,5,6-pentamethyl-acetophenones compared to 2,6-dimethyl- and 2,3,5,6-tetramethyl-acetophenones.

It would similarly be erroneous to conclude that since the first primary band of β-resorcylic acid very nearly coincides with that of *p*-hydroxybenzoic acid, steric effects must be small. This similarity of bands may be fortuitous,

since it is not always observed, and in β-resorcylic acid, compared to *p*-hydroxybenzoic acid, and also in similar types of compounds, two opposing effects operate, which may cancel out. These are, on the one hand, the electrical effect of the hydroxyl group, which will tend to change the wave-length of maximal absorption towards longer wave-length accompanied by increased absorption intensity, and on the other, the steric effect which will act in exactly the opposite manner. Furthermore, as expected for a number of compounds, the steric effect is so prominent compared with the electrical effect as to be readily identified. For example, *p*-chlorobenzoic acid in acid solution absorbs maximally at 241 mμ, $\epsilon = 16{,}300$ (8), while 2,4-dichlorobenzoic acid in acid solution absorbs maximally at 232 mμ, $\epsilon = 7400$ (9). Since steric effects have been postulated to be almost always present, even in the *absence* of a *para*-substituent, one would expect that in the *presence* of a *para*-substituent steric effects on the *ortho*-substituent would almost always be quite large. This follows immediately from the consideration that considerably more energy is required to twist a double bond than is required to twist a single bond (13). Hence the steric effect will be the larger of the two opposing effects and thus trisubstituted benzene derivatives will normally exhibit either a first primary band similar to that of the most displaced band of the constituent compounds or more frequently this same band with a detectable steric effect. Lastly, the steric effect may become so large that the *ortho*-substituent is completely dislodged from the plane of the benzene ring and will then not at all contribute to the observed band. The B-band of the trisubstituted compound will then agree closely with the B-band of the *para*-disubstituted compound, which has in fact been observed by Doub and Vandenbelt (9).

These data therefore reasonably conclusively point to steric phenomena as one of the two main factors towards a general explanation of the location of maximal absorption of the B-band, and in particular are in agreement with our assumptions as stated above.

Secondary Band (C-band)

Although a more general explanation must await the results of further experimental work which is in progress, certain statements about steric effects in C-bands appear justified. These are:

(i) Steric effects can be detected in this band.

(ii) These steric effects are different, inasmuch as apparently (*a*) the C-band is comparatively insensitive to small steric effects; (*b*) larger steric effects are readily apparent, but again different from the steric effects observed in the B-band.

One illustration of this is provided by the sensitiveness to hydrogen-bonding. In the B-band, the evidence for hydrogen-bonding is somewhat inconclusive. In the C-band, however, *ortho*-hydroxy acetophenones and benzoic acids, compared to the corresponding methoxy-compounds, give rise to a much more pronounced effect (see Table IV). It is noted that hydrogen-bonding gives rise to a more pronounced band at longer wave-length, possibly because of

TABLE IV

MAIN ABSORPTION MAXIMA OF SALICYLIC ACID AND RELATED COMPOUNDS IN DIETHYL ETHER (6)

Substituent	Acetophenone				Benzoic acid			
	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}
2-Hydroxy	251	9,700	327	3800	237	7,800	307	4400
4-Hydroxy	267	19,100	—	—	251	18,300	—	—
2-Methoxy	246	8,000	306	2600	~230	8,100	291	3500
4-Methoxy	266	18,000	—	—	251	18,300	—	—

increased rigidity of the molecule. This would also explain the more displaced position of the secondary band of salicylic acid and β-resorcylic acid compared to that of benzoic acid and *p*-hydroxybenzoic acid respectively.

An anomaly, or apparent anomaly, however, might be thought to exist, since salicylic acid compared to *p*-hydroxybenzoic acid exhibits opposite effects in the primary and secondary bands. Therefore, one might argue, if salicylic acid has been postulated to be non-planar, is not planarity now invoked to account for the hydrogen-bond effect? This objection, however, is not valid, since it was stated above (postulate (ii) (*a*)) that the C-band is not sensitive to small steric effects. Hence while the non-planarity might be sufficient to give rise to the B-band effect, it would not be sufficient to upset the typical hydrogen-bonding effect. In other words, although the hydrogen-bond effect in the C-band may be due to increased planarity it does not mean that the increased planarity gives rise to a wholly planar molecule. Furthermore, there is no reason for steric and hydrogen-bond interactions to give rise to identical effects in the B- and C-bands.

Another objection which might be raised is the planarity of salicylic acid in the solid state (5), but to counter this it must be borne in mind that planarity in the solid state does not necessarily involve planarity in the liquid state. For example, diphenyl has been shown to be planar in the solid state also (7), while electron-diffraction data, which have the advantage of giving data concerning the *isolated* molecule, indicate an interplanar angle of $45° \pm 10°$ (1).

Further it seems important to avoid the conclusion that the B-band is associated with separation of charge in the *para*-positions of the excited state and the secondary band with charge separations in the *ortho*-positions. For many compounds this suggestion is quite untenable, and even in favorable instances such as might appear to be provided by the salicylic acid spectra, the hypothesis breaks down. For example, the C-band of salicylic acid should clearly be similar to that of β-resorcylic acid (see Table III).

ACKNOWLEDGMENTS

The authors wish to thank the National Research Council of Canada and the Research Corporation of New York for grants in support of these studies.

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LIGHT ABSORPTION STUDIES

PART IV. THE EFFECTS OF STERICALLY HINDERED CONFORMATIONS ON THE ELECTRONIC SPECTRA (B-BANDS) OF CONJUGATED SYSTEMS[1]

By W. F. Forbes and W. A. Mueller

ABSTRACT

The equation $\epsilon/\epsilon_0 = \cos^2(\theta_1-\theta_2)$ recently proposed by Braude and co-workers is developed to account more rigorously for the spectra of unsymmetrical molecules. The results obtained from the revised equation, $\epsilon/\epsilon_0 = \frac{1}{2}[\cos^2(\theta_1-\theta_2)+\cos^2(\theta_3-\theta_4)]$, support the interference value of hydrogen obtained independently from spectral data, and suggest a re-examination of the reported theories accounting for the spectra of alicyclic enones and dienones, and for steric effects of type I.

INTRODUCTION

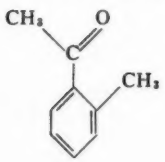
In a recent series of papers, Braude and his collaborators (1, 3, 4, 6) have developed the equation $\epsilon/\epsilon_0 = \cos^2(\theta_1-\theta_2)$ to obtain the value of the interplanar angle from spectral data in sterically hindered compounds. The literature cited in one of these papers (1) reflects the uncertainty which currently prevails concerning the correct assignment of interplanar angles in even diphenyl itself, the spectrum of which has been discussed by a large number of workers. A single equation which could be used to give the roughly correct interplanar angle for a variety of conjugated molecules would therefore be of great significance, and the series of papers by Braude and co-workers in fact provide such an equation.

We are in almost complete agreement with the proposed equation, but have also independently arrived at two conclusions, which lead us to suggest a further development of the above-mentioned equation. These conclusions are that, firstly, our value obtained for the interference value of the hydrogen atom is somewhat larger than that assumed by Braude and co-workers, who accept a value of 0.60 Å for hydrogen. Our own value for hydrogen, the justification of which will be reported in a separate communication, is 0.95 Å, which suggests larger interplanar angles for certain steric conformations than have hitherto been supposed. Our second conclusion concerns our discussion of the spectra of 2-methylacetophenone and 2-methylpropiophenone (7), in which we have considered 2-methylacetophenone, for example, to exist in two different conformations,* IA and IB, which by analogy with the cyclohexenones (see below), we shall refer to as the *s-cis* and *s-trans* forms. We then (7) tentatively concluded that the absorption of 2-methylacetophenone and similar compounds is due to transitions involving chiefly the *s-cis* form (IA). By combining this suggestion with the original formula we are now able to put forward a more complete explanation concerning the mechanism of absorption in sterically hindered conjugated compounds.

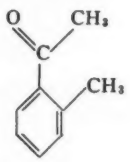
[1]*Manuscript received February 24, 1956.*

Contribution from the Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland. This paper is dedicated to the memory of the late Professor E. A. Braude, D.Sc., F.R.I.C.

**Following Braude (6) we use the terms "configuration" and "conformation" respectively in connection with stereoisomerism involving energy barriers greater and smaller, respectively, than ca. 20 kcal./mole.*



IA
(*s-cis*)



IB
(*s-trans*)

ULTRAVIOLET ABSORPTION SPECTRA AND STERIC CONFORMATIONS

In compounds where the interaction energies of the *s-cis* and *s-trans* forms are identical, for instance the symmetrically substituted acetophenones and benzaldehydes (see Fig. 1) or the *ortho*-substituted diphenyls, we accept the original equation, since considering either *s-cis* or *s-trans* forms, the values of θ_1 and θ_3 will be identical and hence the equation will apply to both forms. It is thus not necessary to consider each form independently.

The same considerations, however, will not apply to molecules like 2-methylbenzaldehyde and 2-methylacetophenone in which the fraction of molecules absorbing in the *s-cis* and the *s-trans* form will not be identical. If we accept the function $\cos^2(\theta_1-\theta_2)$ to be a reasonable measure of the fraction of all molecules in either the *s-cis* or the *s-trans* form undergoing the electronic transition, and then take the average, the simplest equation to combine these two equations is:

$$[1] \qquad \epsilon/\epsilon_0 = \tfrac{1}{2}\{\cos^2(\theta_1-\theta_2)+\cos^2(\theta_3-\theta_4)\},$$

where θ_3 and θ_4 represent the interplanar angles of the ground and excited states respectively of the *s*-form not previously considered. If we further make the additional assumption with Braude that θ_2 and θ_4 are $\sim 0°$, we obtain:

$$[2] \qquad \epsilon/\epsilon_0 = \tfrac{1}{2}(\cos^2\theta_1-\cos^2\theta_3).$$

Since a full definition of all the terms used and their justification has been given in the series of papers already referred to (1, 3, 4, 6), we have confined ourselves to a schematic representation of the electronic transitions for three typical compounds, 2,6-dimethylbenzaldehyde, 2-methylbenzaldehyde, and 2-methylacetophenone (see Figs. 1, 2, and 3), to illustrate our modification. We have included in our figures also another schematic illustration to suggest the possible transitions from various ground states with different interplanar angles. By plotting interplanar angles against probability of absorption, we intend to show the most probable positions in which a molecule in the ground state can absorb light.

While no attempt has been made at this stage to obtain more than a qualitative relationship, we have assumed that in a hindered conformation on approaching coplanarity, the repulsion energy becomes somewhat larger than the gain of energy due to increased resonance. Thus the probability of transition will fall off more sharply as the interplanar angle approaches a planar sterically hindered form than in other directions. We have illustrated this in Figs. 1, 2, and 3, by a steeper slope of the curve in that part of the graph, and also in Fig. 4, using the same diagram as proposed by Braude and Timmons (6).

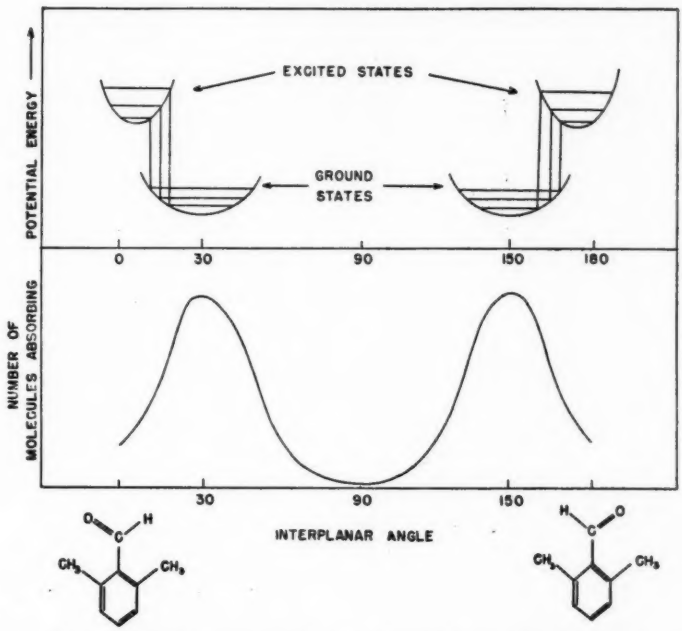


FIG. 1. *Top.*—Schematic representation of electronic transitions between ground and excited states in 2,6-dimethylbenzaldehyde.
Bottom.—Distribution curve for ground state molecules of 2,6-dimethylbenzaldehyde contributing to the observed absorption.

The results obtained from Equation [1] for the new mean interplanar angles of both *s-cis* and *s-trans* forms and the corresponding values obtained by Braude and co-workers are listed in Table I.

It is noted that where different angles are obtained, the differences are not unduly large, and for many of the examples cited (all the symmetrical molecules) the values are of course identical. A number of interesting observations,

TABLE I

INTERPLANAR ANGLES DEDUCED FROM STERIC EFFECTS IN ORTHO-ALKYLATED BENZALDEHYDES AND ACETOPHENONES

Compound	ϵ/ϵ_0	Our values		Comparison value of Braude *et al.* (3)
		s-cis	*s-trans*	
4-Methylbenzaldehyde	1.00	0°	0°	0°
2-Methylbenzaldehyde	0.87	31°	0°	21°
2,4-Dimethylbenzaldehyde	0.94	20°	0°	—
2,6-Dimethylbenzaldehyde	0.78	28°	28°	28°
4-Methylacetophenone	1.00	0°	0°	0°
2-Methylacetophenone	0.58	50°	31°	40°
2,4-Dimethylacetophenone	0.85	25°	20°	24°
2,6-Dimethylacetophenone	0.34	55°	55°	55°
2,4,6-Trimethylacetophenone	0.20	63°	63°	63°

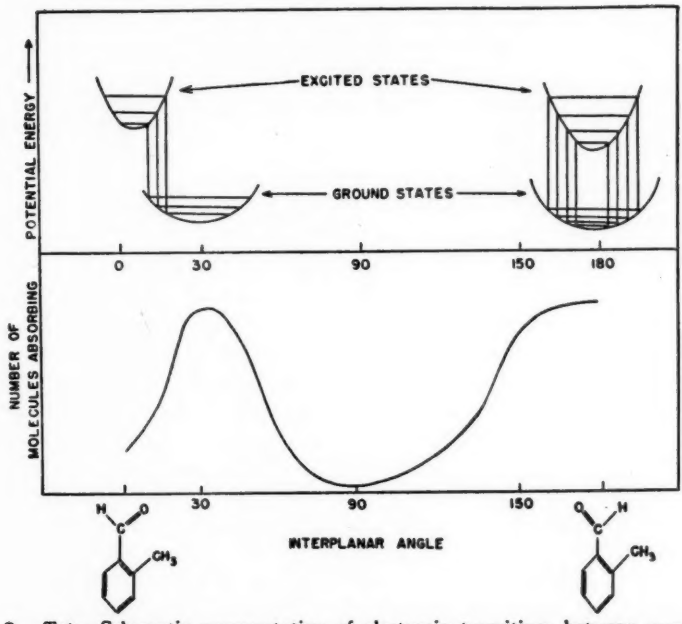


FIG. 2. *Top.*—Schematic representation of electronic transitions between ground and excited states in 2-methylbenzaldehyde.
Bottom.—Distribution curve for ground state molecules of 2-methylbenzaldehyde contributing to the observed absorption.

however, follow from this more detailed treatment thus:

1. The previously noted observation (7) that values of absorption intensities (ϵ) are sometimes halved, when one possible planar form is hindered while the other is not, can be deduced immediately from Equation [1]. This follows since if θ_1 is $\sim 0°$ (i.e. one planar form) and θ_3 is large (i.e. one non-planar form), then $\cos^2\theta_1 \rightarrow 1$ and $\cos^2\theta_3 \rightarrow 0$; hence ϵ/ϵ_0 will tend towards $\frac{1}{2}(1-0) = \frac{1}{2}$, and this therefore explains the observed approximate halving of absorption intensity.

2. Conversely, if an approximately halved intensity of absorption without appreciable change of location of maximal absorption is observed (designated by Braude and co-workers as a "steric effect" of type I and subsequently referred to thus), then this may be taken as an indication that the observed intensity of absorption is due mainly to one of two possible planar forms.

With this observation in mind the spectrum of 1-acetyl-2-methylcyclohexene (II) would appear to be due mostly to the *s-cis* form (IIA) since the intensity of absorption is almost halved relative to that of 1-acetylcyclohexene (III).

Braude and Timmons (6) have recently fully discussed this spectrum as part of their studies on alicyclic ethylenic ketones and on the basis of their equation they have logically concluded that 1-acetyl-2-methylcyclohexene most probably exists with an interplanar angle of about 45° and not chiefly with an interplanar angle of about 180° (*s-cis* form) as suggested by us and

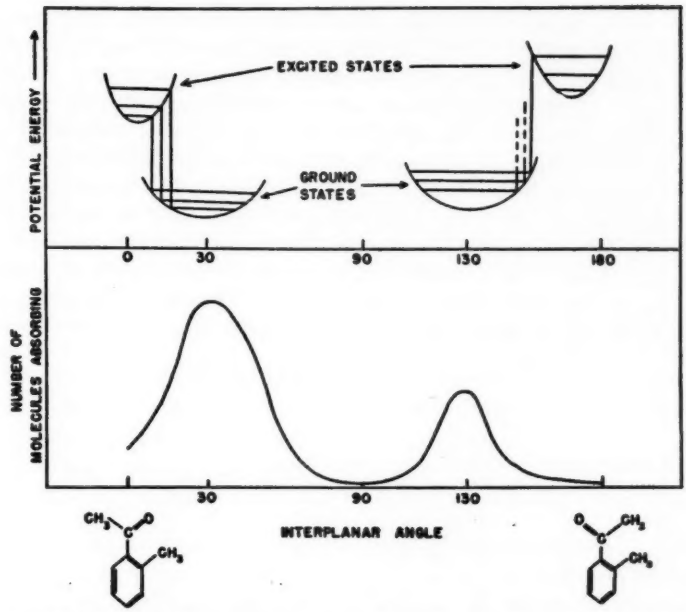
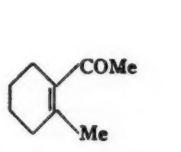


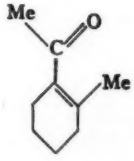
FIG. 3. *Top.*—Schematic representation of electronic transitions between ground and excited states in 2-methylacetophenone.

Bottom.—Distribution curve for ground state molecules of 2-methylacetophenone contributing to the observed absorption.

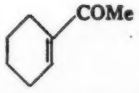


λ_{max} 245 mμ, ϵ = 6500

II



IIA



λ_{max} 232 mμ, ϵ = 12,500

III

also by Turner and Voitle (8). Turner and Voitle conclude that the chromophores in both 1-acetylcyclohexene (III) and 1-acetyl-2-methylcyclohexene (II) are essentially uniplanar, but that whereas the former exists in the *s-trans* conformation, the latter has an *s-cis* conformation. Our interpretation leads us to favor an *s-cis* and *s-trans* conformation for 1-acetylcyclohexene (III) and an *s-cis* conformation only for 1-acetyl-2-methylcyclohexene (II).

This, we suggest, is in fact indicated using the arguments of Braude and Timmons (6) which may be discussed under three headings. The only difference in the treatment is that we shall assume our revised equation, rather than the original equation.

The first argument of Braude and Timmons assumes as probable that the conformation with $\theta_1 = 45°$ will have a lower potential energy (E_0+1 kcal./mole, where E_0 is the energy of the planar *s-trans* system) than that ($E_0+2.5$ kcal./mole) of the conformation with $\theta_1 = 180°$, and that the former will therefore be preferred. The value of E_0+1 kcal./mole is obtained since no hypsochromic displacement greater than 20 Å, equivalent to about 1 kcal./mole, is observed. Assuming our equation, on the other hand, the absorption intensity due to the conformation with $\theta_1 = 45°$ will contribute only little to the total intensity of absorption and hence a shift of even as much as 60 Å, equivalent to *ca.* 3 kcal./mole, may go unnoticed within the main absorption band due to the conformation with $\theta = 180°$. This then leads to the relations as shown in Fig. 4, where the difference between the curves for any value of θ

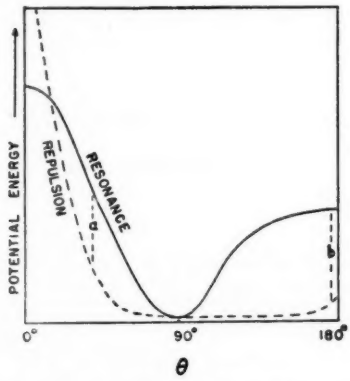


FIG. 4. Dependence of resonance energy and repulsion energy on interplanar angle (schematic). After Braude and Timmons (6).

represents the stabilization energy for that particular conformation. Fig. 4 is so drawn as to show conditions under which this is greater for $\theta = 180°$ (intercept *b*) than for $\theta = 45°$ (intercept *a*).

Braude and Timmons obtain further support for their views by the close agreement between the interplanar angles calculated on the basis of their equation for 1-acetyl-2-methylcyclohexene and 2-methylacetophenone. However, this agreement will equally support our equation, since although the value of 2-methylacetophenone is modified, so is in a similar manner the value for the interplanar angle of 1-acetyl-2-methylcyclohexene.

Finally, support against the *s-cis* conformation is deduced by Braude and Timmons from infrared spectra, since the difference between the ethylenic and carbonyl stretching frequencies is only 57 cm.$^{-1}$, whereas compounds with an enforced *s-cis* configuration consistently give a value of >75 cm.$^{-1}$ for this difference. Although this is clearly an argument against the *s-cis* conformation, we do not consider it a conclusive argument, since the argument does possibly allow for more than one interpretation. For example, 1-acetyl-2-methylcyclohexene will according to our hypothesis exist in the ground state

in forms which will not contribute to the observed ultraviolet absorption spectrum, but which will presumably contribute to the observed infrared spectrum. As it is, the reported value of 1678 cm.$^{-1}$ for the carbonyl stretching frequency of 1-acetyl-2-methylcyclohexene does not preclude an *s-cis* conformation (cf. 7-Oxoergosta-8(14):22-dien-3-yl acetate, 1680 cm.$^{-1}$ (6), which has a fixed *s-cis* configuration); the value of 1621 cm.$^{-1}$ for the ethylenic stretching frequency does suggest a weaker dipole interaction than is in fact observed for other *cisoid*-systems. However, this weakening may be caused by dipole separation due to steric factors; although precisely what the effect of a slightly sterically hindered molecule is on the ethylenic and carbonyl stretching frequencies does not appear to have been fully worked out.

3. Carrying the argument one step further, one would expect that with three double bonds where four *s-cis* and *s-trans* isomers are possible, it might be possible to obtain steric effects of type I corresponding to a reduction of intensity to approximately 75, 50, and 25%, as the number of permitted planar forms is reduced from four to one.

Fortunately such an example—reasonably closely approximating to the above prediction—appears to be available in the β-ionone series as illustrated in Table II.

As the number of planar *s-cis* and *s-trans* forms is progressively reduced by the introduction of methyl-groups; the intensity of absorption appears to be caused almost exclusively by the remaining planar forms. Thus the location of maximal absorption remains fairly constant, while the absorption intensity is reduced very greatly—roughly proportional to the permitted number of planar *s-cis* and *s-trans* isomers (see Table II).

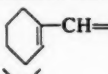
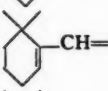
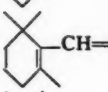
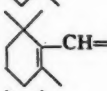
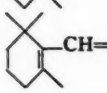
If one were to assume that all the molecules exist in only one *s-cis* or one *s-trans* form while the interplanar angle is progressively increased, a similar ratio of absorption intensities could hardly be accounted for. While the theory of increased interplanar angles, assuming an *s-trans* conformation throughout, could account for the observed changes from (*a*) to (*b*) and from (*d*) to (*e*), it could not easily be invoked to account for the observed intensity changes from (*b*) to (*c*) and from (*c*) to (*d*) which will not affect the interplanar angle of the *s-trans* form (see Table II, Fig. i). A similar argument would also hold if any other conformation were considered to account exclusively for the observed dienone absorption.

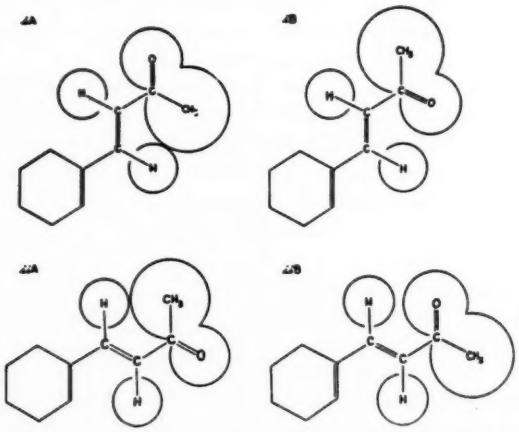
4. The final conclusion which we may draw from the modified equation is, however, probably the most far-reaching. One of the aims of studying the steric effects in ultraviolet light absorption data is to seek an explanation for steric effects of type I as defined previously. One explanation for this phenomenon has been provided by assuming electronic transitions between a non-planar ground state and a near-planar excited electronic state (3, 5).

However, on more closely examining the diagrams either in the above-mentioned paper (3) or in the present communication (see Figs. 1, 2, and 3), it seems likely that as the actual transitions are thus reduced in number, their actual energy values, as estimated from the graph, and even their mean, are no longer identical to the energy values which would represent transitions

TABLE II

ABSORPTION SPECTRA OF β-IONONE AND RELATED COMPOUNDS ACCORDING TO BRAUDE AND JONES (2)

	Compound	Dienone-band		*s-cis* and *s-trans* isomers (i, ii, iii, iv) contributing to absorption (see figures below)
		λ_{max}, mμ	ϵ_{max}	
(*a*)		281	20,800	i, ii, iii, iv
(*b*)		281	13,000	ii, iii, i reduced, iv eliminated
(*c*)		296	10,700	ii, i reduced, iii reduced, iv eliminated
(*d*)		295	9400	ii, i reduced, iii further reduced, iv eliminated
(*e*)		278	4500	ii eliminated, i eliminated, iii and iv as for (*d*)



FIGS. i*A*, i*B* and ii*A*, ii*B* represent the two possible configurations of (i) and (ii). *A* and *B* are not otherwise distinguished, since the —$COCH_3$ group may be considered one unit as a first approximation. (iii) would be as Fig. (ii) except that the —$COCH_3$ group is in the *s-cis* position with respect to the —CH=CH— group. (iv) would be as Fig. (i) except that the —$COCH_3$ group is in the *s-cis* position with respect to the —CH=CH— group, and not in *s-trans* as it is in Fig. (i).

between non-hindered ground and excited states. With this in mind we have somewhat "flattened" our potential energy curves compared to those usually seen in the literature (3, 5) in order to allow for absorption at approximately

the same maximal wave-length, since the theory as described may not be ruled out completely, but should rather be regarded as an alternative explanation of the observed spectral data.

However, another hypothesis to account for steric effects of type I appears to suggest itself. This is, that steric effects of type I are in fact *only* caused by the number of contributing planar or near-planar *s-cis* and *s-trans* forms being reduced. As soon as only one such *s-cis* or *s-trans* form is possible any further steric hindrance will give rise to a steric effect of type II, namely a shift in the location of maximal absorption, accompanied by reduced absorption intensity.

ACKNOWLEDGMENTS

The authors are indebted to the National Research Council of Canada and the Research Corporation of New York for research grants.

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NOTES

THE SYNTHESIS OF INDOLE-3-ACETYL-D,L-ASPARTIC ACID AND RELATED COMPOUNDS[1]

By Norman E. Good

It has recently been shown that plants conjugate indole-3-acetic acid with aspartic acid (1, 4). Moreover unpublished work done in this laboratory indicates that the reaction is not confined to indoleacetic acid. Applications of indole-3-propionic acid and indole-3-butyric acid to plants result in the formation of indolepropionylaspartic and indolebutyrylaspartic acids. Consequently it is to be expected that such compounds will continue to interest biochemists and, since their preparation presents certain problems, a generally applicable method of synthesis has been developed. The classical method of amide formation via the acid chloride proved practically useless for derivatives of indoleacetic acid since the conditions necessary for the formation of indoleacetylchloride also led to its rapid decomposition. The mixed anhydride method of Boissonnas (2) which was used successfully in the preparation of other amides of indoleacetic acid (7) was unsatisfactory with aspartic acid, perhaps because of a competing formation of aspartic anhydride. Eventually it was found that esterification of aspartic acid with benzyl alcohol, condensation of the ester with indoleacetic acid through the use of N,N′-dicyclohexylcarbodiimide (6, 5), followed by reductive removal of the benzyl groups resulted in a good yield of indole-3-acetyl-D,L-aspartic acid. The same method when applied to 2,4-dichlorophenoxy-acetic, indole-3-propionic, and indole-3-butyric acids gave comparable yields of the corresponding aspartic derivatives but, unfortunately, neither indolepropionylaspartic acid nor indolebutyrylaspartic acid has been crystallized as yet.

EXPERIMENTAL

Dibenzyl-D,L-aspartate Hydrochloride

The dibenzyl ester of aspartic acid was prepared by a modification of the azeotropic distillation method of Cipera and Nicholls (3). D,L-Aspartic acid (13.3 gm., 0.1 mole) was suspended in 100 ml. of benzyl alcohol (0.97 mole) containing 22.0 gm. benzenesulphonic acid (0.125 mole) in a round-bottomed flask. The flask was warmed for 5–10 min. on a steam bath by which time nearly all of the amino acid had dissolved. Hot carbon tetrachloride (300 ml.) was added and the cloudy reaction mixture was heated until about 10 ml. had distilled off. The flask was then fitted with a Soxhlet extractor containing a thimble filled with anhydrous magnesium sulphate (25 gm.) and the solution heated under reflux overnight. The mixture was allowed to stand at room temperature for several hours. The benzenesulphonic acid salt of dibenzyl-D,L-

[1]*Contribution No. 77, Science Service Laboratory, Canada Department of Agriculture, University Sub Post Office, London, Ontario.*

aspartate was then removed by filtration, washed once with carbon tetrachloride and several times with dry ether. Residual solvent was removed under vacuum. The yield was 40 gm. (85%). (The salt of dibenzyl-L-aspartate is much more soluble in carbon tetrachloride and only precipitates after the addition of a considerable volume of ether.)

The benzenesulphonic acid salt (40 gm.) was suspended in about 300 ml. dry ether and 14 ml. triethylamine was slowly added with stirring. The suspension was allowed to stand for 0.5 hr. with occasional stirring and was then filtered. The precipitate was resuspended in dry ether containing a little triethylamine and the suspension again filtered. Ether and excess triethylamine were removed from the combined filtrates by distillation at reduced pressure and the residue was taken up in 500 ml. dry ether containing 10 ml. benzyl alcohol. Dry HCl was added slowly in considerable excess. The hydrochloride was then removed by filtration and washed with dry ether. The yield was 29 gm. (83% of the aspartic acid).

*Indole-3-acetyl-*D,L*-aspartic Acid*

Dibenzyl-D,L-aspartate hydrochloride (400 mgm., 1.14 mM.) was suspended in tetrahydrofuran (5 ml.), and triethylamine (0.16 mL., 1.14 mM.) was added slowly with stirring. The mixture was allowed to stand for a few minutes after which it was filtered and the precipitate washed with additional tetrahydrofuran. The combined filtrate and washings were then gently heated on a steam bath in a stream of air until nearly all the tetrahydrofuran had been removed. Indole-3-acetic acid (175 mgm., 1.0 mM.) and 1.0 ml. tetrahydrofuran were added. After the indoleacetic acid had dissolved, the viscous solution was cooled somewhat below room temperature and N,N′-dicyclohexylcarbodiimide (220 mgm., 1.05 mM.) in 0.5 ml. tetrahydrofuran was added with vigorous swirling over five minutes. Residual carbodiimide was washed into the reaction mixture with another 0.5 ml. tetrahydrofuran and the stoppered flask was left overnight at room temperature. Ethyl acetate (10 ml.) was added and N,N′-dicyclohexylurea (215 mgm.) was removed by filtration. The filtrate was extracted successively with 0.1 *N* HCl, 0.2 *N* $NaHCO_3$, and water. The solvents were again removed by gently warming in an air stream. The residue was taken up in 50 ml. of *n*-butanol, and palladium catalyst (5% on charcoal) was added. The suspension was shaken under hydrogen (3 atm.) for four hours, whereupon the catalyst was filtered off and washed with more butanol. The filtrate was extracted once with 0.1 *N* HCl, once with water, and three times with 0.5 *N* $NaHCO_3$ (5, 2.5, and 2.5 ml.). The pooled bicarbonate extracts were in turn extracted with ether and the dissolved ether removed by aeration. The aqueous solution was then acidified to pH 2.0 with 80% phosphoric acid. Indole-3-acetyl-D,L-aspartic acid (165 mgm., 57% of the indoleacetic acid) separated as pink crystals when the acidified solution was left overnight in the refrigerator, m.p. 187°–190° C. After treatment with norite and two recrystallizations from water the product was colorless and melted at 190°–191° C. Calc. for $C_{14}H_{14}O_5N_2$: C, 57.9; H, 4.83; N, 9.66. Found: C, 58.1; H, 4.94; N, 9.56%.

When 2,4-dichlorophenoxyacetic acid was used in place of indole-3-acetic acid a 50% yield of 2,4-dichlorophenoxyacetyl-D,L-aspartic acid resulted. After one recrystallization from 50% alcohol the melting point was 212–214° C. Wood and Fontaine (8) give 217° C. as the melting point of the racemic derivative.

The author wishes to acknowledge the assistance of Mr. R. W. White.

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RECEIVED MAY 17, 1956.
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THE CALCULATION OF THE EXTENT OF ION-PAIR FORMATION IN SOLUTION

BY G. H. DEBUS*

In recent publications (1, 2, 3) extensive use has been made of the Robinson–Stokes equation to evaluate the equivalent conductance of concentrated solutions of strong electrolytes. The agreement between theory and experiment is surprisingly good up to a concentration of about 3 moles per liter.

According to Wishaw and Stokes (6), when the observed conductance is found to be less than the calculated, this must be attributed to ion-pair formation. The results obtained for ammonium nitrate show reasonable constancy of K, the dissociation constant, but the method of Stokes and Wishaw involves laborious calculations; the degrees of dissociation, α, could only be found by a series of approximations and the help of a graph. A graphical and more direct way consists in plotting the experimental and the calculated values (for $\alpha = 1$) of $\kappa\eta/\eta_0$ (product of the specific conductance and the relative viscosity) against the molarity. For equal values of the ordinate the degree of dissociation is obtained by the ratio of the corresponding concentrations.

The mathematical proof of this is as follows: The complete equation for the equivalent conductance, Λ, of a fully dissociated electrolyte is, according to Robinson and Stokes (5):

$$[1] \qquad \frac{1000\kappa}{c} = \Lambda = \left(\Lambda_0 - \frac{B_2\sqrt{c}}{1+B\mathring{a}\sqrt{c}}\right)\left(1 - \frac{B_1\sqrt{c}F}{1+B\mathring{a}\sqrt{c}}\right)\frac{\eta_0}{\eta}.$$

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At constant temperature, and for a fixed solvent and a fixed electrolyte, å, B, B_1, and B_2 are constant, and F varies only with the concentration, c, i.e.

$$F = \frac{\exp(0.2929B\text{å}\sqrt{c}) - 1}{0.2929B\text{å}\sqrt{c}}.$$

Λ is then only a function of the concentration multiplied by the relative viscosity of the solution:

[2] $$1000\kappa/c = \Lambda = f(c)\eta_0/\eta.$$

For an electrolyte that is not fully dissociated c is substituted by αc and

[3] $$1000\kappa/\alpha c = \Lambda/\alpha = f(\alpha c)\eta_0/\eta.$$

By rearranging, the following is obtained from [2] and [3]:

[4] $$1000\kappa\,\eta/\eta_0 = cf(c) = f^1(c)$$

and

[5] $$1000\kappa\,\eta/\eta_0 = \alpha c f(\alpha c) = f^1(\alpha c).$$

The values of $1000\kappa\eta/\eta_0$ for a fully dissociated electrolyte ($\alpha = 1$) are calculated and compared with the experimental values of the weak electrolyte, represented by equation [5].

For each experimental value $\kappa_2\,\eta_2/\eta_0$ of the weak electrolyte, at concentration c_2, there is a corresponding concentration, c_1, of the fully dissociated electrolyte so that (see Fig. 1)

[6] $$1000\kappa_1\,\eta_1/\eta_0 = 1000\kappa_2\,\eta_2/\eta_0$$

and

[7] $$f^1(c_1) = f^1(\alpha c_2)$$

or

$$c_1 = \alpha c_2.$$

The dissociation of the weaker electrolyte at concentration c_2 is equal to c_1/c_2.

A previous method used in this laboratory (3), where α was obtained by the ratio of the experimental value of the equivalent conductance (Λ_2) to the calculated value (Λ_1) at the same concentration, yielded a degree of dissociation which was too high. The deviation increases with the decrease of α.

Indeed, from [2] and [3],

$$\Lambda_1 = f(c)\eta_0/\eta,$$
$$\Lambda_2/\alpha = f(\alpha c)\eta_0/\eta$$

and the concentrations being equal

$$\Lambda_2/\Lambda_1 = \alpha f(\alpha c)/f(c).$$

$f(c)$ decreases with increasing concentration, and consequently at the same concentration $f(\alpha c) > f(c)$, or $\Lambda_2/\Lambda_1 > \alpha$.

The method of equation [5] has been applied to the calculation of the degree of dissociation of the ionization of trichloroacetic acid, a substance which is completely ionized in dilute solution but associates at higher concentration.

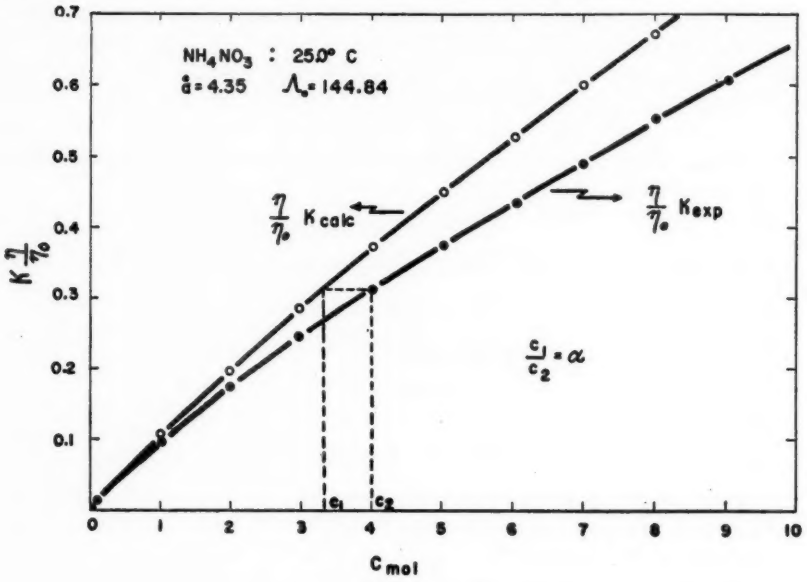

FIG. 1.

The values obtained for the ionization constant (K) showed some variation. This may be explained by the uncertainty in the values of Λ_0, å, γ, and by approximations during calculation and interpolation of experimental values. As mentioned previously a breakdown in the theory is expected at concentration above 3 moles.

RESULTS

The results (4) are contained in Table I.

TABLE I

C_{mol}	Λ_{exp}	Λ_{calc} å = 5.5 Λ_0 = 387.5	$K\eta/\eta_{0exp}$	$K\eta/\eta_{0calc}$	α	K
0.01	—	373.7	—	—	—	—
0.0446	352.7	358.3	0.01601	0.01626	0.983	1.77
0.1010	335.7	341.8	0.03530	0.03600	0.980	3.10
0.1521	323.8	331.2	0.05221	0.05354	0.977	3.78
1.009	207.0	232.2	0.2936	0.3294	0.890	3.56
1.566	156.0	195.9	0.3965	0.4980	0.785	2.24
2.044	121.4	166.3	0.4677	0.6409	0.714	2.65
3.166	67.72	121.3	0.5294	—	0.540	1.01
3.777	46.68	101.0	0.5220	—	0.436	0.82
4.568	28.83	82.3	0.4698	—	0.322	0.63

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RECEIVED MAY 17, 1956.
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THE EFFECT OF ELECTROLYTES ON THE RATE OF CHLORIDE LOSS FROM CHLOROPENTAMMINE CHROMIUM (III) ION IN AQUEOUS SOLUTION

BY M. IKUTA, H. G. MCADIE, and W. MACF. SMITH

We have examined the effect of various electrolytes on the rate of aquation of chloropentammine chromium (III) nitrate,

$$Cr(NH_3)_5Cl^{++} + H_2O \rightarrow Cr(NH_3)_5H_2O^{+++} + Cl^-,$$

with the view of extending data relating to the specific effects of various ions on the rate of reaction. First order kinetics were established for this reaction by Freundlich and co-workers (4).

The nitrate of chloropentammine chromium (III) was prepared by Christensen's method (3) and on analysis showed contents of chromium and chlorine agreeing with the theoretical to within 1 part in 200. The other salts were of reagent grade. The course of the reaction was followed by determining the amount of free chloride in a 5 ml. aliquot by titration with 0.02 molar (*M*) silver nitrate using a differential titration technique (7) involving two silver electrodes connected to an amplifier based on a design of Lyons and Heller (6). Glass stoppered Pyrex volumetric flasks (100 ml. capacity) served as reaction vessels; they were thermostatted in a Sargent bath covered with a black hood.

Preliminary studies at 30° using a concentration of complex salt of about 0.0085 *M* established that heterogeneous reaction and back reaction were negligible and that satisfactory first order plots involving concentration and time were obtained. It was also found that the addition of the nitrates of potassium, sodium, and calcium to 0.12 *M* concentration increased the first order rate constant by about 10%, that the sulphates of both potassium and sodium at 0.06 *M* concentration increased the rate constant by about 55%, and that the sulphate of magnesium at 0.06 *M* concentration increased the rate constant by about 40%. These observations parallel those of Garrick (5) on the aquation of chloropentammine cobalt (III) ion, which indicated that the influence of the added salt is essentially dependent on the nature and concentration of the anion and that the effect of cation is secondary, probably operating only through its influence on ionic strength and to some degree through its ability to associate with the added anions.

The addition of sodium perchlorate led to a slight drop in rate constant for solutions 0.0065 *M* in complex from 1.13×10^{-3} min.$^{-1}$ in the absence of perchlorate to 1.10×10^{-3} at a perchlorate concentration of 0.10 *M*. Addition

of only perchloric acid led to a fairly sharp drop to a rate constant of 1.03×10^{-3} min.$^{-1}$ at an acid concentration of 0.025 *M*. Further increase in acid concentration led to a slight but significant decrease in rate constant almost identical with that produced by addition of sodium perchlorate. Apparently the inhibiting effect of hydrogen ions is substantially absent at concentrations in excess of 0.025 *M* at 30°C.

Further experiments on the effect of added electrolytes involved solutions in which perchloric acid was present in 0.030 *M* concentration and in which one of nitrate, sulphate, iodate, or dichromate of potassium was added to various concentrations. The ionic strength consequently varied. The data are presented graphically in Fig. 1. Some data for the effect of added sodium

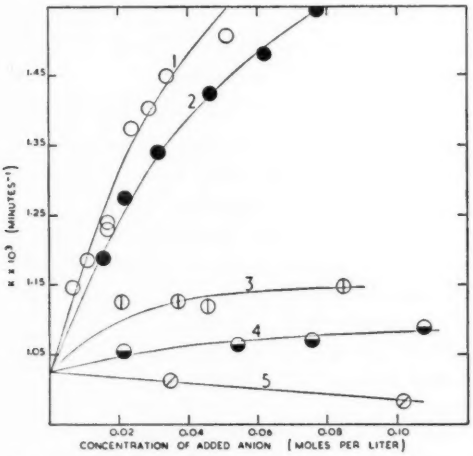

FIG. 1. Effect of added electrolyte on rate constant.

Curve number	Added electrolyte	Curve number	Added electrolyte
1	KIO_3	4	KNO_3
2	K_2SO_4	5	$NaClO_4$
3	$K_2Cr_2O_7$		

All solutions 0.030 *M* in $HClO_4$, 0.0065 *M* in $[Cr(NH_3)_5Cl](NO_3)_2$.

perchlorate are included. The concentrations of nitrate and perchlorate indicated on the figure do not include the contribution of nitrate from $[Cr(NH_3)_5Cl](NO_3)_2$ or of the perchlorate from the perchloric acid. The increases in rate constant accompanying addition of sulphate or nitrate are significantly less than those noted in the experiments in which no perchloric acid was added, e.g. this increase is 45% in the presence of acid compared to nearly 55% in the absence of acid when sulphate was present in a concentration of 0.06 *M*. Some measurements were also made on solutions in which potassium chloride or nitrate was added to various concentrations, perchloric acid was present in 0.030 *M* concentration, and the ionic strength was adjusted to 0.30 with sodium perchlorate. In estimating ionic strength it was assumed that association of sodium or potassium ions with the anions was negligible. The data obtained at constant ionic strength indicated a linear plot of rate

constant against nitrate concentration with a slope of 6.5×10^{-4} min.$^{-1}$ moles^{-1} liter, and also confirmed that chloride has no significant effect on the rate of aquation up to the maximum concentration of chloride investigated, i.e. 0.10 *M*.

From the data given in Fig. 1 it is apparent that sulphate and iodate are much more effective than dichromate in accelerating the rate of aquation and that nitrate has a small positive, and perchlorate a slight depressive, effect. The predominant species in the solutions to which dichromate, iodate, or sulphate was added are $Cr_2O_7^=$, IO_3^-, and $SO_4^=$ but quantitative interpretation of the data is complicated by the equilibria:

$$\begin{aligned} Cr_2O_7^= + H_2O &\rightleftharpoons 2HCrO_4^-, \\ SO_4^= + H^+ &\rightleftharpoons HSO_4^-, \\ IO_3^- + H^+ &\rightleftharpoons HIO_3. \end{aligned}$$

The latter two equilibria operate to reduce hydrogen ion concentration as well as to depress the concentration of the free anion $SO_4^=$ or IO_3^-. We are deferring quantitative interpretation until we have more information about the separate effectiveness of the various anionic species (e.g. $SO_4^=$ and HSO_4^-) in solution, and the influence of ionic strength on this effectiveness.

It is apparent that the variation in rate constant for the aquation reaction with concentration of added electrolyte is not controlled essentially by ionic strength even at low concentrations but is specifically dependent on the nature of the anion. This observation is in accord with the principle first emphasized by Brönsted (2) that only ions of opposite charge can approach sufficiently closely to permit specific interactions to attain importance. We have been unable to detect removal of iodate or sulphate from solution during progress of the aquation reaction but this does not rule out the possibility that these ions are exerting their influence via a bimolecular replacement of chloride followed by a rapid aquation reaction. It might be expected that the effect of perchlorate would be describable in terms of purely electrostatic influences as in the theory of Bateman *et al.* (1) dealing with the influence of ionic strength on the rate of the unimolecular formation of two ions from a neutral molecule. If this were so, and if the mechanism of chloride ions were indeed unimolecular, an increase in the concentration of sodium perchlorate should lead to an increase in rate constant. In fact there is a slight decrease.

ACKNOWLEDGMENT

The authors wish to thank the Committee on Scientific Research of Queen's University for a grant from the McLaughlin Science Fund.

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RECEIVED MAY 25, 1956.
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